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Pharmaceutical policies: effects of financial incentives for prescribers (Review)

Sturm H, Austvoll-Dahlgren A, Aaserud M, Oxman AD, Ramsay CR, Vernby Å, Kösters JP

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TABLE OF CONTENTS

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[Intervention Review]

Pharmaceutical policies: effects of financial incentives for prescribers

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ABSTRACT

Background

Pharmaceuticals, while central to medical therapy, pose a significant burden to health care budgets. Therefore regulations to control prescribing costs and improve quality of care are implemented increasingly. These include the use of financial incentives for prescribers, namely increased financial accountability using budgets and performance based payments.

Objectives

To determine the effects on drug use, healthcare utilisation, health outcomes and costs (expenditures) of policies, that intend to affect prescribers by means of financial incentives.

Search methods

We searched the following databases and web sites: Effective Practice and Organisation of Care Group Register (August 2003), Cochrane Central Register of Controlled Trials (October 2003), MEDLINE (October 2005), EMBASE (October 2005), and other databases.

Selection criteria

Policies were defined as laws, rules, financial and administrative orders made by governments, non-government organisations or private insurers. One of the following outcomes had to be reported: drug use, healthcare utilisation, health outcomes, and costs. The study had to be a randomised or non-randomised controlled trial, interrupted time series analysis, repeated measures study or controlled before-after study evaluating financial incentives for prescribers introduced for a jurisdiction or healthcare system.

Data collection and analysis

Two review authors independently extracted data and assessed study limitations.

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Main results

Thirteen evaluations of budgetary policies and none of performance based payments met our inclusion criteria. Ten studies evaluated general practice fundholding in the UK, one the Irish Indicative Drug Target Savings Scheme (IDTSS) and two evaluated German drug budgets for physicians in private practice. The interrupted time series analyses had some limitations. All the controlled before-after studies (all from the UK) had serious limitations.

Drug expenditure (per item and per patient) and prescribed drug volume decreased with budgets in all three countries. Evidence indicated increased use of generic drugs in the UK and Ireland, but was inconclusive on the use of new and expensive drugs. We found no clear evidence of increased health care utilisation and no studies reporting effects on health. Administration costs were not reported. No studies on the effects of performance-based payments or other policies met our inclusion criteria.

Authors' conclusions

Based on the evidence in this review from three Western European countries, drug budgets for physicians in private practice can limit drug expenditure by limiting the volume of prescribed drugs, increasing the use of generic drugs or both. Since the majority of studies included were found to have serious limitations, these results should be interpreted with care.

PLAIN LANGUAGE SUMMARY

Pharmaceutical policies: effects of financial incentives for prescribers

Drugs make up a major part of the amount of money spent on health care. Today, figures from across the world show that the amount spent on drugs is increasing. Spending more on drugs could mean less money for hospitals, doctors or even schools and other non-health care services. There is, therefore, pressure to control the costs of drugs while maintaining the quality of health care or avoiding the increase in the use of health services.One way for governments, non-government agencies and health insurance companies to try to control drug spending is to influence those who prescribe drugs through financial incentives. This review is about two types of financial incentives that directly affect prescribers: drug budgets and performance based payments (e.g. bonuses or fines to improve prescribing and reduce costs). We included 13 studies from the UK, Ireland and Germany that evaluated budgets, but no studies that evaluated performance based payments.

Budgets are funds that are allocated by payers to a group of or individual physicians, thereby giving them financial responsibility for the management of their own budget. Budgets provide incentives to prescribers to prescribe fewer and less expensive drugs (such as generic drugs). This review found that in these three countries drug spending (per item and per patient) and the volume of drugs prescribed decreased, with more prescribing of generic drugs. There was no clear evidence about the effects of budgets on health care utilization (such as referrals to specialists). The effects on health were not reported in the studies. Overall the evidence for the effects of budgets is weak.

BACKGROUND

(Abbreviations used in this review are listed in Additional Table 1.)

The proportion of total healthcare expenditure spent on drugs has continued to grow in numerous countries over the last decades (Okunade 2006; Reinhardt 2002). For instance in the UK, prescription costs in the 1990s were already the largest element of the Family Health Services budget (Bradlow 1993), and in Spain drug costs in primary care consume over 50% of total primary care expenditure (Antonanzas 2003). Thus policy makers are under pressure to control pharmaceutical expenditures without adversely affecting the quality of care. Unexplained variation in prescribing between individual physicians, different settings and countries (Sturm 2005) and the fact that evidence as reflected in clinical practice guidelines is often not adequately put into practice (Feely 1999), are reasons why regulatory measures targeted at prescribers aim to improve the quality of prescribing.

While policymakers' need for evidence grows, rigorous evaluations

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of regulatory measures are sparse. This review is part of a series of Cochrane reviews of pharmaceutical policies (Aaserud 2006a), investigating the effects of prescribing policies on drug and health care utilisation, costs and health outcomes.

This review focuses on financial policies targeted at prescribers. Policies targeted at prescribers that use educational interventions will be addressed in a separate review.

The general trend to introduce market elements in health care during the last decades has been accompanied by decentralizing decision-making (Bligh 1992; Saltman 2002). For physicians, this has led to an increased accountability for their use of resources (Wilton 1998), including prescribing. Budgetary arrangements for drugs are one prominent example. Regulations also aim to counterbalance market failure and focus on the quality of treatment. Quality-based payments are another type of financial incentive, which are being used increasingly (e.g. in the UK and USA) (Giuffrida 2000; Rosenthal 2006; Rowe 2006; Trude 2006).

Other monetary regulations, such as the remuneration of physicians, can also impact prescribing. However these do not specifically target prescribing and are generally not considered pharmaceutical policies. The restriction of reimbursement for patients might also be considered as a physician centred measure since they affect prescribing by physicians (Kanavos 1999). These policies, however, are considered in other reviews (Aaserud 2006a). Pharmaceutical policies for prescribers that use financial incentives, which are included in this review are therefore limited to drug budgets and quality based payments.

Drug budgets

Budgets are funds that are allocated by payers to a group or individual physicians, thereby giving them financial responsibility for the management of their own budget (Wilton 1998). Budgets therefore encourage economic behaviour and offer incentives for savings. Drug budgets in particular aim at decreasing prescribing costs.

Budgets vary with respect to the level where the budget is set (individual practice or collective budgets), the range of services covered, and the intensity of the incentives (rewards or risks). Additional Table 2 provides a scheme of theoretical models including these three variables.

In general, individual providers or physician representatives and the payer negotiate budgets, depending on whether the budget is on a practice, group or regional/national level. Payers are represented either by a (regional) health authority (UK), a social health insurance scheme (Germany) or, as in the USA, a managed care organization. The budgets are usually based on previous spending, adjusted to patient mix or a defined target (e.g. the average spending of comparable practices, or 1% reduction of overall health care spending, as in Italy). Most budgetary interventions were introduced in the early to mid 1990s and adapted or abolished over time. Budgets provide incentives to prescribe fewer and less expensive drugs. Physicians can modify drug volume by changing the dosage or duration of treatment. Costs per item can be limited by increasing the use of generics or other less expensive drugs with equivalent effects. Theoretically this can also slow down the uptake of expensive new drugs with marginal benefits.

The intensity of the incentive is modified by several factors, one of them being the magnitude of financial risk involved. This can be potential fines (Germany, France) (Mossialos 2005), savings to be used for improvement of medical services as in the UK (Coulter 1993) or Ireland (Walley 2000) or salary bonuses as in Spain or the USA (Antonanzas 2003; Conrad 2004). Incentives are more direct and stronger if applied on an individual level than at a group level and depend on how much the budget level (target) is adapted to provider specific circumstances. For instance in the UK high cost patients and in Germany specific drug classes are exempt (Wilton 1998). The amount, type and timing of prescribing information available to budget holders are important to enable prescribers to react (Schreyögg 2005). Lack of useful information can also be an impediment in effective contracting (Wilton 1998). Low perceived financial risk will decrease the strength of the incentive and depends on the likelihood that fines are actually executed or the ability to influence the results personally versus being dependent on a whole group.

Quality based payments

Quality based payment systems come in a variety of forms. They are most often directed at all physician services and not just at prescribing . Targets for these policies include administrative goals, waiting time, patient satisfaction, diagnostic and treatment goals. Prescribing policies include pay for performance and other policies offering bonuses or penalties to encourage improvement in prescribing. Based on set performance standards physicians are rewarded or punished for their prescribing (McNamara 2005).

Other reviews

We are not aware of any previous systematic reviews on the effects of financial incentives on prescribing. There are some reviews on individual financial policies, like fundholding and the indicative prescribing scheme in the UK (Coulter 1995; Garrison 2003; Gosden 1997; Griffin 1996; Harrison 1996; Schwartz 1996; Smith 1998; Walley 1995) and broad reviews of pharmaceutical policies (Bloor 1996; Ess 2003; Maynard 2003; Mossialos 2004; Narine 1997). Most of those reviews are not systematic.

Other identified reviews focusing on effects of various financial incentives on general medical practice, only occasionally addressed prescribing or reported drug related outcomes. Chaix-Couturier in her literature review of financial incentives, in addition to considering methodological issues, summarized trial results according to the remuneration of physicians and - overlapping - the

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regulations related to managed care (Chaix-Couturier 2000). Effects of interventions on drug-use were reported from only two settings: British fundholding and US managed-care. In the latter case, prescribing was measured as a proxy for quality of care. Reviews investigating the effect of different remuneration systems for physicians (Bloor 1996; Chaix-Couturier 2000; Giuffrida 2000; Gosden 1997; Gosden 2001; Maynard 2003) included only one study out of a total of 25 that reported effects on drug utilisation or related costs (excluding immunization) for: the renewal of prescriptions. Quality-based-payments are a relatively new approach and evaluations are scarce (Giuffrida 2000; McNamara 2005; Roland 2004; Rosenthal 2004).

The aim of this review is to support informed decisions about pharmaceutical policies and to guide future evaluations by preparing an up-to-date, comprehensive summary of what is known from well-designed research about the effects of financial incentives targeted at prescribing on drug use, healthcare utilisation, health outcomes and cost (expenditures). Complementary reviews of other pharmaceutical policies are in progress. The review evaluating effects of pharmaceutical pricing policies is published (Aaserud 2006). It included ten studies of reference pricing and one study of index pricing. Based on the evidence in this review, mostly from senior citizens in British Columbia, Canada, reference drug pricing can reduce third party drug expenditures by inducing a shift in drug use towards less expensive drugs. No evidence of adverse effects on health and no clear evidence of increased health care utilisation was found.

OBJECTIVES

To determine the effects of prescribing policies using financial incentives for prescribers on drug use, healthcare utilisation, health outcomes and costs (expenditures).

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs), non-randomised controlled trials (CCTs), repeated measures (RM) studies (see 'Methods' section), interrupted time series (ITS) analyses, and controlled before-after (CBA) studies.

Types of participants

Health care consumers and providers within a large jurisdiction or system of care. Jurisdictions could be regional, national or international. Studies within organisations, such as health maintenance organisations, were included if the organisation was multi-sited and served a wider population.

Types of interventions

Prescribing policies (financial incentives): Policies that intend to affect prescribing by means of financial incentives for prescribers. Included in this category are management of drug budgets by prescribers, indicative prescribing schemes, and other financial policies for prescribers such as pay-for-performance, if they are specifically targeted at prescribing or drug utilisation.

Policies in this review are defined as laws, rules, financial and administrative orders made by governments, non-government organisations or private insurers. Interventions at the level of a single facility were excluded.

Types of outcome measures

To be included a study had to include an objective measure from at least one of the following outcome categories.

- Drug use (prescribed, dispensed or actually used).
- Healthcare utilisation.
- Health outcomes.
- Costs (expenditures), including drug costs and prices, other health care costs and policy administration costs.

Search methods for identification of studies

The search to identify studies for this review was initially done as a part of a much broader review, Pharmaceutical policies: effects on rational drug use (Aaserud 2006), dealing with the effects of all pharmaceutical policies. The broad review has been split into several reviews, including this one.

Initial broad search for studies of pharmaceutical policies

We developed the search strategy without language restrictions. The following databases were searched:

- Effective Practice and Organisation of Care Group Register, Idealist database searched 22 August 2003
- EBM Reviews, The Cochrane Central Register of Controlled Trials, Third quarter 2003, Ovid, searched 15 October 2003
- MEDLINE Ovid, 1966 to June Week 1 2003, searched 18 June 2003
- EMBASE Ovid, 1980 to 2003 Week 23, searched 18 June 2003

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- CSA Worldwide Political Science Abstracts from 1975 to present, searched 21 October 2003
- EconLit WebSPIRS from 1969 to present, searched 23 October 2003
- SIGLE, System for Information on Grey Literature in Europe, WebSPIRS from 1980 to June 2003, searched 12 November 2003
- INRUD, International Network for Rational Use of Drugs, searched 21 November 2003
- International Political Science Abstracts, WebSPIRS from 1989 to December 2003, searched 9 January 2004
- NHS EED, National Health Services Economic Evaluation Database, CRD, searched 20 February 2004
- PubMed searched 25 February 2004 for relevant journals not indexed in MEDLINE
- NTIS, National Technical Information service from 1964 to present, searched 3 March 2004
- PAIS International, Public Affairs Information Service, WebSPIRS from 1972 to July 2003, searched 23 March 2004
- IPA, International Pharmaceutical Abstract, WebSPIRS from 1970 to December 2003, searched 22 April 2004

The Health Management Information Consortium (HMIC) database was tested and found not to be useful for this review.
In addition, we searched the following web sites and databases:
- World Bank e-Library, searched 4 May 2005
- WHO (World Health Organisation), browsed 25 August 2005
- OECD (Organisation for Economic Co-operation and Development) Publications & Documents, searched 30 August 2005
- SourceOECD, searched 30 August 2005
- World Bank Documents & Reports, searched 30 August 2005

The MEDLINE search strategy was mainly developed using reviews cited in the background section of the protocol and their references. The strategy includes terms for the following categories of interventions:
- Regulation and classification (licensing) policies
- Patent and profit policies
- Marketing policies
- Policies that regulate the provision of drug insurance
- Policies that determine which drugs are reimbursed
- Restrictions on reimbursed drugs
- Prescribing policies
- Pricing and purchasing policies
- Regulation of sales
- Co-payment and caps
- Patient information

We used a modified version of the EPOC search strategy methodology filter to limit the MEDLINE strategy to randomized trials, controlled trials, time series analyses and controlled before-after studies.
Search strategies for most of the other databases were developed on the basis of the MEDLINE strategy.
We screened the reference lists of all of the relevant reports that we retrieved. Authors of relevant papers, relevant organizations, and discussion lists were contacted to identify additional studies, including unpublished and ongoing studies.
We performed a subsequent search for studies of financial incentives for prescribers before publishing this review. Search strategies were developed based on relevant parts and yields of the initial broad search strategy.
MEDLINE (Ovid), 1966 to October Week 1 2005, searched 16 October 2005
EMBASE (Ovid), 1980 to 2005 Week 42, searched 16 October 2005
Global Jolis, online catalogue for the World Bank Country Office PIC/Libraries, searched 19 January 2006
JOLIS, The Library Network serving the World Bank Group and IMF, searched 19 January 2006
WHOLIS, the WHO library database, searched 19 January 2006
ISI Web of Science, searched 28 April 2006 for cited key references

Data collection and analysis

Two authors (of HS, AA, JPK and MOA) independently reviewed all of the search results, abstracts and reference lists of relevant reports. The full text of potentially relevant reports was retrieved (if one or both authors thought it was potentially relevant) and two (of the above) authors independently assessed the relevance of those studies and the limitations of included studies. The lead author (HS) extracted data from included studies in collaboration with one other author (AA, JPK or MOA). For all the steps in the above process disagreements were resolved by discussion, if necessary including another author (ADO).

Included study limitations

We used the standard quality criteria recommended by EPOC to assess the methodological limitations of studies (risk of bias) included in EPOC reviews (Section 6, EPOC 2002).
The criteria for RCTs and CCTs were:
1.concealment of allocation;
2.baseline measurement of outcomes;
3.follow up of professionals;
4.follow up of patients;
5.intention-to-treat analysis;
6.blinded assessment of primary outcomes;
7.reliable primary outcomes measures;
8.other risk of bias.
The criteria for CBA studies were:
1.baseline measurement of outcomes;

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2.baseline characteristics of studies using second site as control;
3.follow-up of professionals;
4.follow-up of patients;
5.reliable primary outcomes measures;
6.blinded assessment of primary outcomes;
7.protection against contamination;
8.other risk of bias.

We used the EPOC definition of RCT, CCT, CBA and ITS studies. For ITS studies the definition is: "The study must have a clearly defined time of intervention AND must have at least three data points before and three data points after the intervention." We also considered designs where there was a control ITS group. Control ITS (CITS) designs are conceptually similar to CBA design but the addition of multiple time points pre and post intervention decreases the likelihood of secular change bias.

Based on experience with two previous systematic reviews (Davey 2005, Grilli 2002), the statistical editor of EPOC, who is also a co-author of this review (CR), suggested minor revisions to the original EPOC criteria for ITS (and RM studies) reported in Ramsay 2003. These consisted of defining reanalysed studies as meeting the 'analysed appropriately' criterion and allowing studies that had at least 12 monthly data points pre and post to meet the 'reason for number of data points' criterion since this allows seasonal effects to be investigated. These criteria more accurately reflect the chance of bias in the study effect sizes. We therefore used the following criteria.

1. The intervention was independent of other changes (protection against secular changes). This was "MET" if there were compelling arguments that the intervention occurred independently of other changes over time and the outcome was not influenced by other confounding variables/historic events during study period.
2. Data were analysed appropriately. This was "MET" if autoregressive integrated moving average (ARIMA) models were used OR time series regression models were used to analyse the data and serial correlation was adjusted/tested for OR reanalysis performed.
3. Reasons for number of data points were given. This was "MET" if data for 12 months (or more) pre- and post-intervention was used OR reason for the number and spacing of data points is given OR sample size calculation performed.
4. Shape of the intervention effect was pre-specified. This was "MET" if point of analysis was the point of intervention OR a rational explanation for the shape of intervention effect was given by the authors. Where appropriate, this should include an explanation if the point of analysis was NOT the point of intervention.
5. Intervention unlikely to affect data collection (protection against detection bias). This was "MET" if it is reported that intervention itself was unlikely to affect data collection (for example, sources and methods of data collection were the same before and after the intervention).
6. Blinded assessment of primary outcome(s). This was evaluated as protection against detection bias. This was "MET" if the authors stated explicitly that the primary outcome variables were assessed blindly OR the outcome variables were objective, e.g. length of hospital stay, drug levels as assessed by a standardised test.
7. Completeness of data set. This was "MET" if the data set covered 80-100% of total number of participants or episodes of care in the study.
8. Reliable primary outcome measure(s). This was "MET" if two or more raters with at least 90% agreement or kappa greater than or equal to 0.8 OR the outcome was obtained from some automated system e.g. length of hospital stay, drug levels as assessed by a standardised test.
9. Other risk of bias.

For CITS (controlled ITS) and CRM (controlled RM) studies, the time series part of the studies were assessed independently from the control part, using the above described criteria for ITS and RM studies. The control series part of the study was assessed using the CBA criteria above. If the control part had serious limitations, it was not included and the study was classified as ITS or RM, otherwise the control data were used as a control in the review.

Overall limitations for each main outcome within each study was assessed by each of the data extractors using the following guidelines:

- No serious limitations = low risk of bias = all criteria scored as 'met'
- Some limitations = moderate risk of bias = one or two criteria scored as 'not clear' or 'not met'
- Serious limitations = high risk of bias = more than two criteria scored as 'not clear' or 'not met'
- Fatally flawed = study results that we believed to be untrustworthy based on an overall judgment of the risk of bias in the study, based on all of the criteria used to assess the risk of bias.

Studies rated as "fatally flawed" were excluded from the review but listed with the reason for exclusion in the Characteristics of excluded studies table. Some setting dependent judgment (i.e. judgment dependent on knowledge of the setting in which a study was done) was used when assessing overall limitations. Where setting dependent judgment has been used, the explanations are provided in Additional Table 3.

Data extraction

We extracted the following additional information from included studies using a standardised data extraction form.

- Type of study (randomised trial, non-randomised trial, repeated measures study, interrupted time series, controlled before-after).
- Study setting (country, key features of the healthcare system and concurrent pharmaceutical policies).
- The sponsors of the study.
- Characteristics of the participants (consumers, physicians, practices, hospitals, etc.).
- Characteristics of the policies.

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- Main outcome measures and study duration.
- The results for the main outcome measures.

If duplicate results from one of the four outcome groups (drug use, health, health care utilisation and costs) were presented, these were included if they provided additional information, which improved understanding or lead to different conclusions from the original paper.

Tables were prepared for each sub-category of intervention including the following information: study identification, characteristics of the intervention, results on drug use, healthcare utilisation, health outcomes, and costs. These tables form the basis for the primary qualitative analyses. In Table 4 and Table 5 we provide a summary of all results per outcome. We also described potential mechanisms through which the policies were intended to affect drug use and costs and postulated mechanisms for other effects, both intended and unintended. In addition we briefly listed and described important policy options for which no evaluations were found.

We attempted to identify important factors that might be taken into consideration by anyone contemplating implementing any of the policy alternatives, including: possible trade-offs (of the expected benefits versus harms and costs), different effects of varying policy conditions and background situations, short versus long term effects, limitations of the available evidence and other important factors that might affect the translation of the available evidence into practice in specific settings.

Our confidence in the available estimates of effects was graded using a modification of the approach recommended by the GRADE Working Group (GRADE 2004). When grading the quality of evidence, we started out grading ITS and RM studies as 'Moderate' quality, and CBA studies as 'Low' quality. This reflects our impression that the results of ITS and RM studies were more compelling (more likely to be correct) than those of CBA studies. The GRADE quality scores are High, Moderate, Low, and Very low.

The following potential explanatory factors were considered: differences in the characteristics of the policies, differences in the settings and differences in study limitations. However, there was an insufficient number of comparisons for similar outcomes across studies to allow for meaningful exploration of heterogeneity.

CBA studies

For CBA studies we reported relative effects. For continuous variables we have reported, if possible, the relative change, adjusted for baseline differences in the outcome measures; i.e. [(the absolute post-intervention difference between the intervention and control groups - the absolute pre-intervention difference between the intervention and control groups) / the post-intervention level in the control group]. In the case of UK fundholding results were analysed separately for short-term (usually one year pre to one year post) and long-term (two to up to four years) effects.

ITS and CITS studies

The preferred analysis method for ITS (and RM) studies was either a regression analysis with time trends before and after the intervention, which adjusted for autocorrelation and any periodic changes, or ARIMA analysis. The results for the outcomes should be presented as changes along two dimensions: change in level and change in slope. Change in level is the immediate effect of the policy and is measured as the difference between the fitted values for the first post-intervention data point (one month after the intervention) minus the predicted outcome one month after the intervention based on the pre-intervention slope only. The relative change in level was calculated by dividing the change in level by the predicted outcome one month after the intervention based on the pre-intervention slope only and multiplying by 100%.

Change in slope is the change in the trend from pre to post intervention that reflects the "long" term effect of the intervention. Since the interpretation of change in slope could be difficult, we chose to present the long-term effects similar to the way we calculated and present the relative immediate effects. We presented the effects after half a year as the difference between the fitted value for the sixth month post-intervention data point (half a year after the intervention) minus the predicted outcome six months after the intervention based on the pre-intervention slope only and dividing by the predicted outcome six months after the intervention based on the pre-intervention slope only and multiplying by 100%. The effects after one year and two years were measured similarly. For drug expenditures we also calculated the savings after a half year, one and two years as the area between the predicted expenditures curves and the actual expenditures.

Given that policy changes are often announced some months prior to official implementation, a transition phase is often defined as the six months from official announcement. If applied, all results excluded the transition phase data. However, if studies provided only few data points, if the data itself did not suggest a transition phase, and most importantly, if the authors did not state a transition phase, it was not applied. Transition phase was used in one study of this review (Harris 1996).

If papers with ITS design did not provide an appropriate analysis or reporting of results, but presented the data points in a scannable graph or in a table, we (CR, AV) reanalysed the data using methods described in Ramsay 2003. The following segmented time series regression model was specified: Y(t) = B0 + B1*Pre-slope + B2*Post-slope + B3*intervention + e(t) where Y(t) is the outcome in month t. Pre-slope is a continuous variable indicating time from the start of the study up to the last point in the pre-intervention phase and coded constant thereafter. Post-slope is coded 0 up to and including the first point post intervention and coded sequentially from 1 thereafter. Intervention is coded 0 for pre-intervention time points and 1 for post-intervention time points. In this model, B1 estimates the slope of the pre-intervention data, B2 estimates the slope of the post-intervention data and B3 estimates the change in level of outcome as the difference between the estimated first point post intervention and the extrapolated first point post intervention if the pre-intervention line was continued into the post-intervention phase. The difference in slope is calculated

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by B2-B1. The error term e(t) was assumed to be first order autoregressive. For CITS studies, the difference between the relative changes of the intervention and the control groups are presented. Confidence intervals (95%) were calculated for all effect measures. For studies that were analysed as CBA by the authors and reanalysed as CITS by the reviewers, results were presented for both methods, however for grading the quality of evidence, only the ITS analyses were used.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

The main literature search (for all pharmaceutical policies, not only pricing policies) using electronic databases and web sites resulted in 17.000 references to sift. The updated search for prescribing policies, including MEDLINE, EMBASE and Science Citation Index, resulted in 3521 additional references, including reference lists from relevant studies and reports. Roughly estimated we sifted 20.000-21.000 references in total. We identified and retrieved in full text a total of 189 papers that were potentially relevant for this review. Papers retrieved covered the following interventions: budgetary policies, remuneration of physicians (capitation, fee for service), and pay for performance (including target payments). If the study intervention qualified as a pharmaceutical policy and specifically targeted prescribing behaviour, many still were excluded because they did not meet the study design inclusion criterion. They were primarily reviews, editorials, modelling studies, cross-sectional studies, and before and after studies without a control group. The Characteristics of excluded studies table provides reasons for exclusion of those studies for which it is plausible to expect that a reader would question why the study was not included, studies that are well known but do not meet all of the inclusion criteria, and ITS studies that meet all the inclusion criteria except that there were too few data points.

We identified four studies (Dusheiko 2003; Elhayany 2001; Etter 1997; Houghton 1998) that might meet our inclusion criteria, but these could not be retrieved and assessed before submission of the review. The studies are listed amongst 'Studies awaiting assessment' in the reference list.

Sixteen papers, reporting 13 studies, met the inclusion criteria. In 10 studies the effects of British fundholding were analysed (Baines 1997c; Bradlow 1993; Burr 1992; Corney 1997; Harris 1996; Kammerling 1996; Rafferty 1997; Whynes 1997; Wilson 1995; Wilson 1999). One study analysed effects of the indicative prescribing scheme in Ireland (Walley 2000). Two studies reported on drug expenditure budgets in Germany (Guether 1995; Schöffski 1997). Three studies were reported in more than one paper (Bradlow 1993; Schöffski 1997; Wilson 1995). See the Characteristics of included studies table for details.

Study designs

None of the studies were RCTs or CCTs or RM studies. We included three CITS analyses (Harris 1996; Rafferty 1997; Wilson 1995), three ITS (Guether 1995; Schöffski 1997; Walley 2000) and nine CBA studies (Baines 1997c; Bradlow 1993; Burr 1992; Corney 1997; Harris 1996; Kammerling 1996; Rafferty 1997; Wilson 1995; Wilson 1999). Three of those are presented as CBA and CITS studies (Harris 1996; Rafferty 1997; Wilson 1995). All time series results were re-analysed by the review-team (AV, CR). See 'Characteristics of included studies' table.

Characteristics of the setting and interventions of included studies

Although budgetary policies were applied in at least seven countries (see Table 6), evaluations could be included from only three (UK, Ireland and Germany) (see Table 3).

UK fundholding

Fundholding for general practitioners (GPs) in England and Scotland was introduced with the first wave of voluntary practices in April 1991 and in Wales and Northern Ireland in April 1993. Each year practices with initially at least 11,000 registered patients could join the fundholding scheme in "waves", until in 1997 health care-trusts were introduced. With each wave, regulations on requisites for joining practices were relaxed. The aim of fundholding was to increase efficiency of care by giving GPs financial control over some of their provided services (Audit Comm. 1996; Glennerster 1996; Glynn 1992; Weiner 1990; Wilson 1995). Besides costs of prescribed drugs, practice staff and a range of secondary care such as specialist services and elective surgical services were covered by separate budgets, with the drug budget offering the greatest savings potential (Harris 1996). Overspending in one budget had to be covered by funds from another budget, savings could be used in other areas of patient care (Coulter 1993). Budgets were set based on previous expenditure and at the discretion of the local health authority medical advisor. Therefore budgets varied substantially from practice to practice (Day 1991). Concurrently all practices, fundholders and non-fundholders alike were exposed to practice level feedback with their own performance in comparison with others (benchmarking), as well as to regular visits of independent pharmaceutical advisors of the local health authority . Additionally initiatives to reduce costs of individual prescriptions such as limited lists and the promotion of generics were launched (Baines 1997).

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UK Indicative prescribing scheme

Introduced at the same time as fundholding (Bligh 1992; Dep. of health 1989; Mannion 2005; Wilson 1995) and with budgets calculated in the same way, indicative budgets meant, there was only a virtual budget without penalty for overspending. The practices could not individually retain the surplus, however, up to 50% of the savings could be used by the regional Family Health Authority for improvement of the regions' primary care. Thus, this scheme provided common savings as the only incentive. The schemes were also referred to as indicative prescribing amounts / budgets. Indicative prescribing budgets later became an integrated element of the primary care trusts.

Indicative Drug Targeting Savings Scheme (IDTSS)

In 1993 in Ireland a comparable scheme called Indicative Drug Targeting Savings Scheme (IDTSS) was introduced (Walley 2000). GPs individual indicative or hypothetical budgets covered prescribing and associated costs and were calculated based on previous spending and the national average (Walley 2000b). Savings were split between the GP and the local health authority to be used for the development of services. There were no penalties for overspending.

German drug budget

Collective budgets for drug expenditures for physicians in private practice in Germany were in use from 1993 to 2002 with the stated goal to maximize effectiveness by using less costly and more effective drugs. It was expected that while generic use would increase use of drugs with disputed effect would decrease (Busse 1996; Gross 1994; Henke 1994; Schreyögg 2005; Schwartz 1996; Schwermann 2003). While spending caps were regionally negotiated or nationally set each year and made all physicians in private practice in one region collectively liable, target volumes for each individual practice were only theoretically established. From 2002 budgets were abolished and replaced by practice level target volumes (negotiated between the physician association (KV) and insurers). No studies evaluating this regulation were included. Parallel to the budgets, reference pricing, changing levels of co-payment and price cuts for pharmaceuticals were introduced.

Characteristics of outcomes

Prescribing data in the UK in all studies was obtained from PACT (Prescribing analysis and cost) data, which records costs and numbers of all dispensed NHS prescriptions of general practitioner practices (Majeed 1997). Volume and costs were measured per patient or per adjusted patient unit (PU). PU accounts for increased drug requirements in older patients; Astro-PU additionally corrects for sex and temporary residents (see abbreviation list in Additional Table 1). Changes in costs are also presented per item. An item is defined as each preparation on the prescription.

In Germany included studies are based on data from regional databases providing information of computerized general practitioners and internists in private practice. Data collected were referrals to specialists and hospitals as well as total number of prescriptions.

The Irish data were derived from a regional health authority's GMS (General Medical Services) payments database. Prescribing data, related to individual physicians, was reported quarterly for groups of doctors.

Results are presented with short-term and long-term effects (when available) in Additional Table 7 to Table 8, and summary of findings can be found in Additional Table 4 and Table 5.

Risk of bias in included studies

The quality of included studies is presented in Additional Table 3. For British fundholding drug use was assessed in six CBA studies (Bradlow 1993; Burr 1992; Rafferty 1997; Whynes 1997; Wilson 1995; Wilson 1999), two ITS (Harris 1996; Wilson 1995), and one CITS study (Rafferty 1997). Drug expenditure was assessed by nine CBA studies (Baines 1997c; Bradlow 1993; Burr 1992; Corney 1997; Harris 1996; Rafferty 1997; Whynes 1997; Wilson 1995; Wilson 1999), and the same two ITS and one CITS studies. One CBA study that assessed referrals was included (Kammerling 1996). We reanalyzed all time series data.

All British CBA studies were assessed to have serious limitations due to marked differences between the experimental and control groups (selection bias). Most importantly fundholding was voluntary and requirements to join the scheme especially in the first years made it likely, that fundholders were a selected group with respect to practice size, affluence, location and pre-fundholding levels of prescribing (Coulter 1993; Gosden 1997; Moon 2002). Additionally numerous simultaneous interventions were introduced in both settings, which could not be accounted for in a CBA design. All ITS studies were recalculated based on graphs provided in the publications, therefore of those studies (Harris 1996; Rafferty 1997; Wilson 1995) both CBA and (C)ITS results are provided. Three studies (Harris 1996; Rafferty 1997; Wilson 1995) were assessed as having some limitations.

One ITS study assessed volume and drug costs of the Irish Indicative Drug Targeting Savings Scheme (IDTSS). The quality was rated as having some limitations. We included two ITS studies that evaluated German drug budgets. Drug volume was assessed by one (Guether 1995) and referrals by two (Guether 1995; Schöffski 1997). The quality of these data was rated as having some limitations since data were quarterly rather then monthly and timeseries had too few datapoints (Guether 1995), or due to limitations of the data completeness (Schöffski 1997). In Guether 1995 data was reported with a "quasi control group" (prescriptions for privately insured patients not subject to budgets as opposed to socially insured), but the groups were found to be too different to be used

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as reliable comparisons, and therefore only the ITS data of the intervention group was used in the analysis.

Effects of interventions

Ten studies reported in 12 papers on British fundholding, one study in one paper reported on Irish IDTSS and two studies in three papers of German drug budgets met inclusion criteria. Of all included studies data on drug use was provided by 12 studies of which generic prescribing was reported in six studies, data on drug expenditures based on dispensing by 10 studies and health care utilisation (referrals) by three studies. Detailed results for the included studies are provided in the Table 7 to Table 8, and the summary of evidence can be found in Table 4 and Table 5. Confidence intervals (CI) could only be calculated for ITS results. For CBA results there were not enough data to calculate CIs.

British fundholding

Drug expenditure (Additional Table 7 and Table 9)
Eight studies provided data or information to calculate estimates of the one-year and two-year effect on drug expenditure of fundholders relative to non-fundholders.
(1)--Drug expenditures per item
Mean costs for dispensed drugs per item in British fundholding were reported in four CBA studies of which CITS results were obtained for two studies. All measured outcomes (except one (Wilson 1995, CBA, long term follow up: 0.34)) showed that the real expenditure level of fundholders relative to the expected level dropped more post intervention than those of non-fundholders. Relative changes in levels of fundholders compared to controls for the two CITS studies ranged from -49.17% to- 6.18% at one year follow up (Rafferty 1997; Wilson 1995), and showed mostly a statistically significant, slight increase for longer follow-up periods. Relative effects in CBA studies reporting results at one-year follow-up (Bradlow 1993; Rafferty 1997) ranged from -6.3% to -5.3% for all waves.
(2)--Drug expenditures per patient
Almost all available effects on costs per patient (reported in eight CBA and three CITS studies), across different waves and follow-up periods, consistently showed a bigger relative reduction in expenditure levels in fundholders. Relative level changes of fundholders compared to controls for CITS studies ranged from -79.7% to 66.8% with a median of -2.8% at one year follow up (Harris 1996; Rafferty 1997; Wilson 1995). While most confidence intervals crossed no relative change, some relative changes became statistically significant in long-term follow-up, and effects mostly increased over time. The effect appears somewhat smaller in later waves. CBA results of the same studies were in line with these findings with a median of -4.2 % and a range between -9.5% and 0.5% after 12 months (Baines 1997c; Bradlow 1993; Burr 1992; Corney 1997; Harris 1996; Rafferty 1997; Whynes 1997; Wilson 1995).
(3)--Total prescribing cost
The only study reporting changes in total prescribing costs (Harris 1996) found reductions for most follow-up periods and waves (range at 12 months follow-up: -27.3% to -69.6%), though only third wave results were significant at 12 months.
Drug use (Additional Table 10 and Table 11)
Seven studies provided data or information to calculate estimates of the one-year and two-year effect on drug use by fundholders relative to non-fundholders, and 6 studies reported on generic prescribing
--Overall drug use
Four studies reported effects in 1st wave FH in GB (Burr 1992; Bradlow 1993; Rafferty 1997; Wilson 1995); three reported of later waves (Rafferty 1997; Wilson 1995; Wilson 1999). In CITS (median at 12 months -1.5%; range: -28.8% to +1.5%) as well as in CBA studies (median at 12 months: -1.2%; range: -5.7% to +1.8%) a relative reduction of prescribed drugs in fundholders compared to controls was seen. The effect seemed to decrease with later waves.
--Generic drug use
The effect on generic drug use was the most consistent across waves and follow-up periods: all results reported in two CITS studies and 5 CBA studies uniformly showed a greater increase in use of generic drugs in fundholders, although effects of CITS were not statistically significant (Rafferty 1997: median at 12 months: +15.0% (range -43.7% to 190.5%); at 24 months: +18.3% (13.6% to 23.0%); Wilson 1995). Effects of CBA studies ranged between 8.8% and 13.4% (median: 11.1%) at 12 months (Bradlow 1993; Rafferty 1997), and between 4.0% and 17.2% at 24 months (Baines 1997c; Bradlow 1993; Rafferty 1997; Wilson 1995; Wilson 1999): (median: 10.6%).
--Use of specific drug subgroups
One included CBA study (Wilson 1999) reported the effect on the use of newer or more expensive drugs for gastric ulcer and depression. In both cases the use of newer drugs was relatively lower in fundholders, however this was more pronounced for proton-pump inhibitors (adjusted relative change: -7.9%) than for selective serotonin-reuptake inhibitors (SSRIs) (relative change: -0.8%).
Health
No study reported effects on health.
Health care utilisation (Additional Table 12)
One CBA study (Kammerling 1996) found a decreased relative referral rate to NHS outpatient care for fundholders over long-term follow-up (-15.3%).
Irish indicative drug target savings scheme (IDTSS):
Drug expenditures (Additional Table 13)
One ITS study evaluated the effects of IDTSS (Walley 2000). While the change in costs per item over time was statistically non-significant (relative change in level at 12 months: 0.6%), over-

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all prescribing costs had decreased absolutely. Compared with the expected level without the policy change, the level was reduced at 12 months (-18.0%) and at 24 months (-21.7%) after the introduction of indicative budgets. However these results were also statistically non-significant.

Drug use (Additional Table 14)

A relative reduction in number of prescribed items over a follow-up period of one year (-8.2%) and two years (-10.1%) was found (Walley 2000).

German drug budget

Two German studies were included (Guether 1995; Schöffski 1997) and reanalysed as ITS with some limitations.

Drug expenditures

No evaluations of cost effects of the German drug budget met our inclusion criteria.

Drug use (Additional Table 15)

One (ITS-) study (Guether 1995) provided results on the overall number of prescriptions.

The measured level relative to the expected level decreased from -11.2% at three months to -13.4 % at 12 months). All results were statistically non-significant.

Health care utilisation (Additional Table 8)

Referral rates of socially insured patients to outpatient specialists were reported in two studies (Guether 1995; Schöffski 1997) and were inconclusive (relative effects: -15.4% to 13.2% at 12 months). One study (Schöffski 1997) reported results on referrals to hospital with a relative immediate effect at 3 months of 13.30%, and 13.31% at 12 months.

UK Indicative prescribing scheme

Only one study was identified (Bateman 1996), but did not meet our inclusion criteria. The study indicated that the prescribing behaviour of the general practitioners in the study was similar to that of the fundholding practitioners, and that the incentive scheme did not seem to reduce the quality of prescribing.

DISCUSSION

Although prescribing policies based on financial incentives are applied in various countries (see Additional Table 6), studies that met the inclusion criteria for this review came from only three countries and evaluated only budgetary policies. Cross-sectional studies evaluating modifying factors such as practice characteristics did not meet our study design criterion for inclusion (see Characteristics of excluded studies table), but did provide relevant information (Wilson 1995) that is considered in the discussion below.

Additional Table 4 and Table 5 provide summaries of the main findings. The evidence about the effects of budgetary policies is strongest in British fundholding, although also there the quality of the evidence is graded very low. Drug expenditures (per item and per patient) and the amount prescribed decreased under budgets in all three settings. There is evidence about increased use of generic drugs from the UK and Ireland, while the effect on newer and expensive drugs is inconclusive and the evidence is weak. There is only weak and inconclusive evidence available about the effects of drug budgets on referrals.

Drug budgets - Effects on drug expenditure

Firstly it was assessed, whether drug budgets would limit drug expenditure as intended. Included studies reporting effects on costs were from the UK and Ireland. British fundholders consistently had slower increases in the cost per item than non-fundholders. This effect was found in first wave fundholders (five studies, including two CITS) as well as in later waves (two (CITS) studies) and persisted during longer follow-up (three studies, including one CITS). Costs per patient reported in eleven UK studies also increased at a slower rate in fundholder practices and the effect persisted with longer follow-up. The only included evaluation of indicative budgets (IDTSS) indicated a decrease in the growth rate of overall drug expenditures while maintaining constant costs per item over time (Walley 2000). A decrease in drug expenditure was also reported by other, not included studies from the UK (Mannion 2005), (Burr 1992) as well as in Germany, a different health care system with vastly different budgetary arrangements (Schreyögg 2005).

Drug budgets - Effects on drug utilisation

Lower costs per item indicate use of generic drugs or other less costly drugs. In eight included studies from the UK and Ireland generic drug use consistently increased at a faster rate with budget holding. We expected that this effect would decrease over time, since a switch to generics can only happen once per patient (Walley 2004). Our results, however, did not support that: the effects for long-term follow up were comparable (in CBA studies) and even increased over time (Rafferty 1997).

Evidence from included studies about substitution with other drugs is less strong. It was anticipated, that the proportion of expensive, newer drugs for the same indications would decrease under budgetary arrangements. Only one British study met our inclusion criteria (Wilson 1999) and results showed that overall drug costs and overall number of drugs per patient grew slower in fundholders for two indications (anti-ulcer medication and antidepressant use). While the proportion of the more expensive prescribed proton-pump inhibitors (PPI) grew slower in fundholders, the proportion of SSRI's for depression developed equally rapidly. Lower costs per patient can be achieved by reducing the amount or duration of prescribed drugs. Ranges and the majority of in-

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dividual outcomes of included British studies on dispensed items per patient point to a slower increase of the number of dispensed drugs with fundholding. Also the result from the evaluation of Irish IDTSS (Walley 2000) showed a non-significantly slower growth of drug use over time. Similarly, evidence from the included German study with some limitations showed that prescriptions for patients subject to budgetary constraints decreased while effects for privately insured patients were smaller. Thus drug budgets appear to have decreased prescribing volume in all three settings.

Drug budgets - Effects on health care utilisation

Referrals, the only health care utilisation outcome reported, were measured as an indicator of cost shifting rather than as a surrogate measure of effects on health, and it is important to note that these effects are likely due to a budget for referrals rather than to a drug budget. In the UK it was expected, that referrals within the NHS might decrease since those were subject to the budget and their reduction would offer potential savings to be used for service improvement. To compensate for that, it was expected that physicians would increase referrals to private specialists, not included under the budget (Coulter 1993) and by this create better care structures for their patients (Moon 2002). Results of studies that did not meet the inclusion criteria did not support these claims (Surender 1995). Three studies (Coulter 1993; Gosden 1997; Howie 1995; Maxwell 1993) found neither lower referrals to NHS specialists in fundholding practices nor a change in referrals outside the NHS. However these studies have to be considered with care as control or intervention practices were partly in the preparatory phase for fundholding. Croxson (Croxson 2001) suggested that the apparent lack of effect could also be due to pre-fundholding inflation of referrals. This is supported by a study of prospective fundholders (before and after negotiating budget setting), that assessed referrals in old-age psychiatry (Fear 1994). Only one study reporting referrals met our inclusion criteria (Kammerling 1996) and it found that fundholders indeed slowed down referrals to NHS orthopedic specialist outpatient care as compared to non-fundholders.

In Germany by contrast, referring patients to a higher level of care would save physicians prescribing costs billed to their budgets, so an increase was expected for socially insured patients, but not for privately insured patients without budgetary constraints.

This was not clearly supported by the evidence included in our review. The two results for socially insured patients both found a statistically non-significant increase in referrals, but at one-year follow-up the results were contradictory (Guether 1995; Schöffski 1997). The absolute effects for privately insured patients assessed by Güther (Guether 1995) were smaller but paralleled the overall development. These findings are supported by descriptive data reported by Schöffski 1997.

Quality of care and modifying factors

Effects on quality of care

No studies reported effects on health outcomes or the quality of prescribing. The effect on treatment quality can therefore only be estimated indirectly. In theory, quality might suffer if necessary treatment were withheld or postponed. The reduction found in prescriptions in all settings could indicate a potential quality problem. In Germany however, descriptive nationwide data indicate that the overall decrease of prescriptions after the introduction of the budgets was mainly due to a reduced use of drugs with disputed effectiveness, such as expectorant drugs, medication against dementia and medication to treat neuropathies (Schreyögg 2005). Evidence about the use of expensive new drugs in all settings is inconclusive. Evidence is clearest for the increased use of generic drugs, which is generally considered to be "quality neutral" (Walley 2004); that is, would not be expected to have an impact on the quality of care or health outcomes.

Changes in referrals to other sectors might be the result of under treatment. At the same time, however, quality might increase by the involvement of specialist care (Schreyögg 2005). With UK fundholding the change in referral patterns (Ess 2003; Narine 1997; Walley 2004) might have induced additional local health care capacities (Coulter 1995; Glynn 1992), thus possibly having a positive effect on quality, although the creation of a two-tear system was feared. Several excluded studies reported newly created clinics at health centres and reduced waiting times, making organisation of care more effective (Bain 1993; Croxson 2001; Jones 1993; Kammerling 1996). However, again, this was probably not attributable to drug budgets, but to fundholding for referrals.

Evidence from this review does not clarify effects on quality of care or health outcomes.

Savings

We did not find direct evidence about generated savings. The slower increase in drug expenditure with budget holding, at least over the first year of follow-up, potentially generated savings. Wilson for instance, based on regional British results, calculated hypothetical national savings over the first three years of fundholding to be £72 million (Wilson 1995). However this effect of fundholding was perceived as minor relative to the continuing absolute increase in spending (Stewart-Brown 1995, see Bradlow 1993). National drug expenditures still grew more than the government's forecast during the first two years of the policy (Jones 1993). Sustainability has also been questioned based on the results of an excluded study (Rietveld 2002; Stewart-Brown 1995). The results of this review, however, do not indicate a decrease in effect for longer follow-up periods.

In Germany national trends in sales or turnover are difficult to interpret due to German reunification. However, sickness fund expenditures decreased markedly after the introduction of the budgets in 1992 for drugs with disputed effects, while expenditures for drugs with undisputed effects continued to rise (Schreyögg 2005). On the other hand the demonstrated increase of referrals

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could offset generated savings as indicated by Schöffski (Schöffski 1997).

Modifying factors

Different factors may modify the effects, but studies of modifying factors are generally cross-sectional and did not meet our inclusion criteria. The magnitude of the financial risk, which can be postulated to be a key-modifying factor, is dependent on the absolute budget level, the directness of potential savings, costs or losses involved, and the range of services covered under the budget.

Since budgets usually are set based on previous levels of prescribing, an anticipatory increase of prescribing was feared but could not be clearly confirmed by evidence from the UK (Coulter 1995; Croxson 2001; Healey 1994; Stewart-Brown 1995) or Germany. Some authors have concluded that irrespective of changes in prescribing, UK fundholders were more often able to keep within their budgets (Jones 1993). However since the strictness of negotiated budgets was very inconsistent and fundholding budgets generally considered generous (Glynn 1992), this evidence is weak (Robinson 1996). In Germany Guether 1995 attributed the increase in prescriptions in the three Autumn months before the start of the policy to anticipatory hoarding by patients, while seasonal variation cannot be excluded by the presented data.

Other modifying factors include the health care setting and other concurrent policy changes. In the UK, for instance, benchmark information along with virtual budgets was also introduced for non-fundholding practices, while in Germany this information was unavailable. In the UK regular visits by independent pharmaceutical advisors of the local health authority were introduced and Health Promotion Clinics (DMP) were included in the 1991 GP contract (Stewart-Brown 1995). Pharmaceutical detailing activities might be different in the two countries. In Germany patients could change their GP or attend any specialist if the expected medication was not prescribed (Schwermann 2003), while in the UK, where GPs act as gatekeepers for specialist care patients might have a closer bonding (HitCP-UK 1999). In Germany co-payments of drugs were changed repeatedly (Schwermann 2003). Other potential modifying factors include reference-pricing (Schwermann 2003), other drug pricing and formulary regulations, practice characteristics and marketing effects (Stewart-Brown 1995) (see Additional Table 16).

From the available evidence it is not possible to distinguish the impact of any of these modifying factors (Coulter 1995). Therefore there is substantial uncertainty concerning the transferability of results to other settings.

Methodological issues/limitations

Comparability of the presented results, even from within one country, is limited due to the following aspects. (1) Studies from the UK used different units (e.g. per prescribing units (PU) and per patient, median or mean). (2) Prescribing volume was mostly measured in dispensed items per patient, where a change in the true volume (for example, shorter prescriptions or lower dosage) cannot be detected. However, a systematic change in item size between fundholders and non-fundholders during the study periods is not to be expected (Wilson 1995).

In the UK, selection bias was likely because of specific practice characteristics of fundholders such as practice size (Dixon 1994; Moon 2002). Other relevant characteristics mentioned were training status, deprivation score (Whynes 1995) and the possibility to dispense (Rafferty 1997; Whynes 1995). The risk of selection bias for all CBA results of fundholding might lead to an overestimation of the effect. The same was true for the study populations of the included German studies, where only computerized practices were included.

If possible, CBA studies were reanalysed as ITS studies. Although the effect sizes cannot be directly compared the consistence of the effect direction over time strengthens the evidence.

Evidence from this review is largely in accordance with common interpretations of fundholding effects in the UK. While overall drug expenditure continued to grow, fundholders seemed to be able to contain prescribing costs slightly better (Bloor 1996; Ess 2003; Mannion 2005; Narine 1997; Walley 2004; Wilson 1995). This effect seems to be partly the result of switching to generics or other less expensive drugs (Bloor 1996; Ess 2003; Gosden 1997; Narine 1997; Walley 2004), and partly due to decreased prescribing volume (Gosden 1997; Narine 1997; Rietveld 2002; Walley 2004). The effects might decrease over time (Bloor 1996; Rietveld 2002), however the evidence clearing this review does not support this.

Results of the review also support conclusions from narrative reviews (Bloor 1996; Schwermann 2003; Walley 2004) about the German collective budget. Overall prescriptions decreased immediately after introduction of the spending caps. No German data on cost and generic use met our inclusion criteria. Commonly the decrease in drug expenditure along with increased generic use (Bloor 1996; Walley 2004) was at least partly attributed to the drug budgets, despite other concomitant interventions such as price cuts and co-payments (Walley 2004). No studies with long-term follow-up met our inclusion criteria. The effects of budgetary policies in New Zealand have been interpreted similarly (Bloor 1996).

AUTHORS' CONCLUSIONS

Implications for practice

Although financial incentives are considered to be an important element of strategies to change prescribing patterns (Grol 2000; Rutledge 1996) only studies on budgetary policies from three countries met our inclusion criteria. Due to methodological limitations, overall the evidence is weak. It supports the conclusion that drug budgets can decrease prescribed drug volume and drug

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expenditure. Results on health care utilisation and quality of care were inconclusive. Administration costs were not reported.

Implications for research

Our review found few well-designed evaluations of pharmaceutical prescribing policies. Although we performed an extensive literature search, there could be additional studies in the grey literature, such as working papers or internal government reports that we have not identified. Updates of this review will include further efforts to identify studies in the grey literature.

Compared to budgetary policies elsewhere, British fundholding has been relatively extensively evaluated, albeit with important limitations. Some of the studies included in this review could be recalculated as ITS (with controls in the UK setting), but authors mostly presented controlled before after designs for drug use, drug costs and health care utilisation outcomes. Such observational designs have serious limitations. No randomised trials were conducted. However well done studies, including trials could be applied to evaluate drug policy interventions if planned in advance. They might be done more quickly and efficiently than observational studies, and could reduce the risk of bias (Schneeweiss 2004).

Evaluations in the majority of included studies focus on relatively short term outcomes. Longer-term analyses would provide important supplementary evidence, but the risk for bias related to other confounding interventions increases with the length of the observation period.

Because pharmaceutical policies have uncertain effects and they might cause harm as well as benefits, it is important that they are properly evaluated. Evaluations should be planned ahead of introducing the policies and should be a routine part of the policy process.

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* *Indicates the major publication for the study*

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Baines 1997c

Methods	CBA SERIOUS LIMITATIONS
Participants	Setting: UK, Linconshire and Devon Fundholders (FH) (1st - 3rd wave) Lincolnshire:19 Devon: 22 Non-FH: Linc:86/ Devon: 106 Unit: Practice
Interventions	UK, NHS Fundholding
Outcomes	Drug use (generics) Costs (per patient)
Notes	Only long term effect reported in analysis since data for wave 1 to 3 has been aggregated by author***

Bradlow 1993

Methods	CBA SERIOUS LIMITATIONS
Participants	Setting: UK, Oxford FH (1st wave): 5 Non-FH: 7 Unit: Practice
Interventions	UK, NHS Fundholding
Outcomes	Drug use: (Items, generics) Costs (per patient, per item) Cost: Total net cost, per 1000 PU, Mean cost per item, Net cost per 1000 PU , Mean cost per item
Notes	Dispensing group excluded from analysis since not comparable with control group

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Burr 1992

Methods	CBA SERIOUS LIMITATIONS
Participants	Setting: UK, Mid- Glamorgon FH (1st wave): 4 Non-FH: 4 Unit: Practices
Interventions	UK, NHS Fundholding
Outcomes	Drug use (Items) Costs (per patient)
Notes	

Corney 1997

Methods	CBA SERIOUS LIMITATIONS
Participants	Setting: UK, South Thames Region FH (2nd wave): 4 Non-FH:4 Unit: Practice
Interventions	UK, NHS Fundholding
Outcomes	Costs (per patient)
Notes	1st wave experimental group excluded because no baseline

Guether 1995

Methods	ITS SOME LIMITATIONS
Participants	Setting: West Germany Statutory health insurance General practitioners: 82 Unit: GPs
Interventions	German drug budget
Outcomes	Drug use (prescriptions) Health care utilisation (referrals)
Notes	

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Harris 1996

Methods	CBA/ CITS SERIOUS /SOME LIMITATIONS
Participants	Setting: UK, England All general practices Unit: Practice Unit: Practice
Interventions	UK, NHS Fundholding
Outcomes	Drug use (items) Costs (per patient)
Notes	

Kammerling 1996

Methods	CBA SERIOUS LIMITATIONS
Participants	Setting: UK, District Health Authority in South West England FH (2nd and 3rd wave): 10 Non-FH: 22 Units: Practice Fundholders 2nd and 3rd wave: 10 Non- fundholders: 22 Units: Practice
Interventions	UK, NHS Fundholding
Outcomes	Healthcare utilization (referrals) hospitals
Notes	1 year post not included in analysis because baseline/ intervention data mixed for 2nd and 3rd wave

Rafferty 1997

Methods	CBA/ CITS SERIOUS /SOME LIMITATIONS
Participants	Setting: UK, Northern Ireland FH (1st wave): 23 FH (2nd wave): 34 FH (3rd wave): 9 Non-FH: All in Northern Ireland Unit: Practice Fundholding 2nd wave: 34 Fundholding 3rd wave: 9 Non- fundholders: All in Nortern Ireland Unit: Practice

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Rafferty 1997 (*Continued*)

Interventions	UK, NHS Fundholding
Outcomes	Drug use (prescriptions, generics) Costs (per patient, per item)
Notes	

Schöffski 1997

Methods	ITS SOME LIMITATIONS
Participants	Setting: Germany, Statutory Sickness Funds 309- 382 practices Unit: Practice
Interventions	German drug budget
Outcomes	Healthcare utilization: Referral rate, hospitalisation rate
Notes	

Walley 2000

Methods	ITS SOME LIMITATIONS
Participants	Setting: Ireland, Eastern Health Board cohort of 223 General practitioners Unit: GPs
Interventions	Ireland Indicative Drug Targeting Savings Scheme (IDTSS)
Outcomes	Drug use (Items) Cost: (per item, per patient)
Notes	Cohorts merged

Whynes 1997

Methods	CBA SERIOUS LIMITATIONS
Participants	Setting: UK, Lincolnshire FH (4th wave): 23 Non-FH: 63 Unit: Practice

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Whynes 1997 (*Continued*)

Interventions	UK, NHS Fundholding
Outcomes	Drug use: (items, generics) Costs: (per patient)
Notes	Wave 1- 3 (aggregated) not included in analysis because no adeqate baseline/ intervention period

Wilson 1995

Methods	CBA/ CITS SERIOUS /SOME LIMITATIONS
Participants	Setting: UK, North West Regional Health Authority FH (1st wave): 20 FH (2nd wave): 31 FH (3rd wave): 49 Non-FH: 312 Unit: Practice
Interventions	UK, NHS Fundholding
Outcomes	Drug use: (items, generics) Cost: (per patient, per item)
Notes	

Wilson 1999

Methods	CBA SERIOUS LIMITATIONS
Participants	Setting: UK, 5 health Authorities in NW-Region
Interventions	UK, NHS Fundholding
Outcomes	Drug use: (DDD, drug subgroups) Cost: (per patient, per DDD)
Notes	

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Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Bain 1993	No control group
Baines 1997	Cross-sectional
Baines 1997b	No baseline data
Bateman 1996	Observational study/ no control group
Chernew 2000	No baseline/ no control group
Coulter 1993	Not adeqate control group
Danzon 1997	Multiple interventions measuered simultanously, effects of drug budgets can not be extractet separately
Edgar 1999	No baseline data
Fear 1994	Evaluated only a pre-fundholding pilot project, with no real incentives
Hoopmann 1995	Cross sectional
Howie 1995	Evaluates a "shadow fundholding" project, pre-fundholding. Overlaps with the start of real fundholding
Jünger 2000	No control group
Malcolm 1999	No control group
Malcolm 2001	No control group
Maxwell 1993	Evaluates a "shadow fundholding" project, pre-fundholding. Overlaps with the start of real fundholding
Newton 1993	No control group
Schreyögg 2004	Untrustworthy data because of time series strongly influenced by historical event (Germany reunification)
Schreyögg 2005	
Whynes 1995	Untrustworthy results, intervention groups are at different stages of fundholding
Whynes 1997b	No control group

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DATA AND ANALYSES

This review has no analyses.

ADDITIONAL TABLES

Table 1. Abbreviations

CBA	Controlled before and after
CCT	Controlled clinical trial
CI	Confidence interval
CITS	Controlled interrupted time series
CRM	Controlled repeated measures
DMP	Disease management program
EPOC	Effective Practice and Organisation of Care
FH	Fundholding (fundholders)
H2RA	Histamine-2 receptor antagonist
GP	General Practitioner
Item	is defined as each preparation on the prescription
ITS	Interrupted time series
IDTSS	Indicative Drug Target savings scheme (Ireland)
NIC	Net ingredient costs
OECD	Organisation for Economic Co-operation and Development
PACT	Prescribing analysis and cost (data used in British fundholding)
PPI	Proton pump inhibitors
PU	Prescribing unit, allows for demographic differences between practices. Patients under 65 are counted as one prescribing unit, while those aged 65 and over count as three. AstroPU in addition corrects for age, sex and temporary residency
RCT	Randomised controlled trial
RM	Repeated measures

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Table 1. Abbreviations (*Continued*)

RR	Risk ratio (intervention vs control group)
RR (adj)	Risk ratio (adjusted for pre intervention differences) = RR post intervention / RR pre intervention
SSRI	Selective serotonin reuptake inhibitors
WHO	World Health Organisation

Table 2. Description of interventions of included studies

COUNTRY	POLICY/TIME PERIOD	MOTIVATION	SETTING OF BUDGET	PHYSICIAN INCENTIVES	PHYSICIAN DISINCENT.	THEORETICAL EFFECTS
Germany	Collective drug budget "spending caps" (Health Care Reform Act) 1993-2002 (Formally abolished in 2001)	Control prescription drug cost	Based on previous regional spending. From 1998: regional net budget= gross budget minus co-payments and rebates from industry nationally set 1993, then regionally Negotiated between physician associations and statutory health insurances	None (savings will not be available to physicians)	Regional physician associations are responsible for overspending (max 5% of total budget). Can decline to pay for excess spending and can request it from individual practice	Reduction of drugs with disputed effect, savings can facilitate use of more expensive drugs. Improve quality of prescribing. Increase referrals to save (drug budget is independent of other care)
	Individual practice caps "Target volumes" 2002-	Control prescription drug cost	Of gross budgets a target expenditure per patient is calculated and extrapolated to a praxis level (adjusted for instance for specialty and patient age) Negotiated by physician associ-	None	Excessive spending will have to be paid back (Individual practice monitoring)	Reduction of drugs with disputed effect, savings can facilitate use of more expensive drugs. Improve quality of prescribing. Increase referrals to save (drug budget is independent of

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Table 2. Description of interventions of included studies (*Continued*)

			ations and statutory health insurances			other care)
UK	Indicative prescribing scheme 1991-1997	Control prescription drug cost	Based on previous spending practice Negotiated by local medical advisors and statutory health insurances	Savings to be used within health authority and equally divided by all GPs to improve services	None	Decrease prescribed drug volume and cost per item. Improve quality of prescribing
Ireland	IDTSS (Indicative Drug target savings scheme) 1993-	Control prescription drug cost	Individual practice budget based on previous spending and national average Negotiated by local medical advisor and practice	Savings were divided between GP and health authority	None	Decrease prescribed drug volume and cost per item. Improve quality of prescribing
UK	Fundholding GB + Scotland: april/1991-1997 (announced in 1990) Wales + Northern Ireland 1993-1997	Control prescription drug cost	Based on previous spending of practice adjusted for patient mix and spending of comparators. Negotiated by local health authority and practice	Savings can be invested by each fundholder to improve services in other budgets, or in the following year following year's drug budget	Responsible for overspending up to a limit of 5000£. Overspending can be covered by other budgets	Decrease prescribed drug volume and cost per item. Improve quality of prescribing. Referrals are postponed, since those are also part of a budget

Table 3. Assessment of limitations in included studies

POLICY: UK FUNDHOLDING									
ITS/ CITS									
STUDY ID	Intervention independent of	Appropriate data analysis	Reason for number and spac-	Shape of Intervention effect	Intervention	Blinded assessment	Blinded assessment	Other risk of bias	Overall assessment

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Table 3. Assessment of limitations in included studies (*Continued*)

	other changes		ing of data-points	pre-specified	unlikely to affect data collection	of primary outcome (s)	of primary outcome measure(s)		of limitations / study design
outcome: DRUG USE (volume)									
Harris 1996	NOT MET*	MET	NOT MET**	MET	MET	MET	MET	NOT RELEVANT	SOME LIMITATIONS
Rafferty 1997	NOT MET*	MET	NOT MET**	MET	MET	MET	MET	NOT RELEVANT	SOME LIMITATIONS
Wilson 1995	NOT MET*	MET	MET	MET	MET	MET	MET	NOT RELEVANT	SOME LIMITATIONS
outcome: DRUG USE (generics)									
Rafferty 1997	NOT MET*	MET	NOT MET**	MET	MET	MET	MET	NOT RELEVANT	SOME LIMITATIONS
Wilson 1995	NOT MET*	MET	MET	MET	MET	MET	MET	NOT RELEVANT	SOME LIMITATIONS
outcome: COSTS									
Harris 1996	NOT MET*	MET	NOT MET**	MET	MET	MET	MET	NOT RELEVANT	SOME LIMITATIONS
Rafferty 1997	NOT MET*	MET	NOT MET**	MET	MET	MET	MET	NOT RELEVANT	SOME LIMITATIONS
Wilson 1995	NOT MET*	MET	MET	MET	MET	MET	MET	NOT RELEVANT	SOME LIMITATIONS

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Table 3. Assessment of limitations in included studies (*Continued*)

* coinciding interventions									
** Not enough data points									
CBA									
STUDY ID	Baseline measurements	Baseline characteristics	Follow-up of professionals	Follow-up of patients	reliable primary outcome measure (s)	Blinded assessment of primary outcome (s)	Protection against contamination	Other risk of bias	Overall assessment of limitations / study design
outcome: DRUG USE (volume)									
Bradlow 1993	MET	NOT MET*	MET	NOT RELEVANT	MET	MET	MET	NOT MET**	SERIOUS LIMITATIONS
Burr 1992	MET	NOT MET*	MET	NOT RELEVANT	MET	MET	MET	NOT MET**	SERIOUS LIMITATIONS
Rafferty 1997	MET	NOT MET*	MET	NOT RELEVANT	MET	MET	MET	NOT MET**	SERIOUS LIMITATIONS
Whynes 1997	MET	NOT MET*	MET	NOT RELEVANT	MET	MET	MET	NOT MET**	SERIOUS LIMITATIONS
Wilson 1995	MET	NOT MET*	MET	NOT RELEVANT	MET	MET	MET	NOT MET**	SERIOUS LIMITATIONS
Wilson 1999	MET	NOT MET*	MET	NOT RELEVANT	MET	MET	MET	NOT MET**	SERIOUS LIMITATIONS

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Table 3. Assessment of limitations in included studies (*Continued*)

outcome: DRUG USE (Generics)									
Baines 1997	MET	NOT MET*	MET	NOT RELE-VANT	MET	MET	MET	NOT MET**	SERIOUS LIMITA-TIONS
Bradlow 1993	MET	NOT MET*	MET	NOT RELE-VANT	MET	MET	MET	NOT MET**	SERIOUS LIMITA-TIONS
Rafferty 1997	MET	NOT MET*	MET	NOT RELE-VANT	MET	MET	MET	NOT MET**	SERIOUS LIMITA-TIONS
Wilson 1995	MET	NOT MET*	MET	NOT RELE-VANT	MET	MET	MET	NOT MET**	SERIOUS LIMITA-TIONS
Wilson 1999	MET	NOT MET*	MET	NOT RELE-VANT	MET	MET	MET	NOT MET**	SERIOUS LIMITA-TIONS
outcome: COST									
Baines 1997	MET	NOT MET*	MET	NOT RELE-VANT	MET	MET	MET	NOT MET**	SERIOUS LIMITA-TIONS
Bradlow 1993	MET	NOT MET*	MET	NOT RELE-VANT	MET	MET	MET	NOT MET**	SERIOUS LIMITA-TIONS
Burr 1992	MET	NOT MET*	MET	NOT RELE-VANT	MET	MET	MET	NOT MET**	SERIOUS LIMITA-TIONS
Corney 1997	MET	NOT MET*	MET	NOT RELE-VANT	MET	MET	MET	NOT MET**	SERIOUS LIMITA-TIONS
Harris 1996	MET	NOT MET*	MET	NOT RELE-VANT	MET	MET	MET	NOT MET**	SERIOUS LIMITA-TIONS

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Table 3. Assessment of limitations in included studies (*Continued*)

Rafferty 1997	MET	NOT MET*	MET	NOT RELEVANT	MET	MET	MET	NOT MET**	SERIOUS LIMITATIONS
Wilson 1995	MET	NOT MET*	MET	NOT RELEVANT	MET	MET	MET	NOT MET**	SERIOUS LIMITATIONS
Wilson 1999	MET	NOT MET*	MET	NOT RELEVANT	MET	MET	MET	NOT MET**	SERIOUS LIMITATIONS
outcome: REFERRALS									
Kammerling 1996	MET	NOT MET*	MET	NOT RELEVANT	MET	MET	MET	NOT MET**	SERIOUS LIMITATIONS
CONTROL PART OF THE CITS STUDIES, FOR INPUT IN THE OVERALL ITS SCORE IN THE TABLES ABOVE									
ALL OUTCOMES									
Harris 1996	MET	NOT MET*	MET	NOT RELEVANT	MET	MET	MET	MET	SOME LIMITATIONS
Rafferty 1997	MET	NOT MET*	MET	NOT RELEVANT	MET	MET	MET	MET	SOME LIMITATIONS

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Table 3. Assessment of limitations in included studies (*Continued*)

Wilson 1995	MET	NOT MET*	MET	NOT RELE-VANT	MET	MET	MET	MET	SOME LIMITA-TIONS
*All studies appear to have a high risk of bias inherent in the policy: FH are volunteers, contamination due to varying periods of joining for non-FH as for FH									
**Effect size might be underestimated due to simultaneous incentive scheme for controls									
POLICY: IRELAND IDTSS									
ITS/ CITS									
STUDY ID	Intervention independent of other changes	Appropriate data analysis	Reason for number and spacing of datapoints	Shape of Intervention effect pre-	Intervention unlikely to affect data	Blinded assessment of primary outcome	Data set complete / reliable pri-	Other risk of bias	Overall assessment of limitations

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Table 3. Assessment of limitations in included studies (*Continued*)

				specified	collection	(s)	mary outcome measure(s)		/ study design
outcome: DRUG USE (volume)									
Walley 2000	NOT SURE*	MET	NOT MET**	MET	MET	MET	MET	NOT RELEVANT	SOME LIMITATIONS
outcome: COSTS									
Walley 2000	NOT SURE*	MET	NOT MET**	MET	MET	MET	MET	NOT RELEVANT	SOME LIMITATIONS
outcome: DRUG USE (volume)									
Walley 2000	NOT SURE*	MET	NOT MET**	MET	MET	MET	MET	NOT RELEVANT	SOME LIMITATIONS
*Not discussed in paper									
**Too few data points									
POLICY: GERMAN DRUG BUDGETS									
ITS									
STUDY ID	Intervention independent of	Appropriate data analysis	Reason for number and spac-	Shape of Intervention ef-	Intervention unlikely to	Blinded assessment	Data set complete /	Other risk of bias	Overall assessment

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Table 3. Assessment of limitations in included studies (*Continued*)

	other changes		ing of data-points	fect pre-specified	affect data collection	of primary outcome (s)	re-liable pri-mary out-come mea-sure(s)		of limita-tions / study de-sign
outcome: DRUG USE (vol-ume)									
Guether 1995	NOT MET*	MET	NOT MET**	MET	MET	MET	MET	NOT RELE-VANT	SOME LIMITA-TIONS
out-come: RE-FERRALS									
Guether 1995	NOT MET*	MET	NOT MET**	MET	MET	MET	MET	NOT RELE-VANT	SOME LIMITA-TIONS
Schoeffski 1997	NOT MET*	MET	MET	MET	MET	MET	NOT SURE***	NOT RELE-VANT	SOME LIMITA-TIONS
* Several policies in-troduced simultane-ously (for ex-ample ref. price and copay)									
**Too few data points									
***Fluc-tuation in database, missing data									

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Table 3. Assessment of limitations in included studies (*Continued*)

CONTROL PART OF THE CITS STUDIES, FOR INPUT IN THE OVERALL ITS SCORE IN THE TABLES ABOVE									
STUDY ID	Baseline measurements	Baseline characteristics	Follow-up of professionals	Follow-up of patients	Reliable primary outcome measure(s)	Blinded assessment of primary outcome (s)	Protection against contamination	Other risk of bias	Overall assessment of limitations / study design
ALL OUTCOMES									
Guether 1995	NOT MET*	NOT MET**	MET	MET	MET	MET	MET	MET	SERIOUS LIMITATIONS*** ***
*Differences found in the baseline measurement									
**Different study populations in experimental and control groups									

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Table 3. Assessment of limitations in included studies (*Continued*)

***Not included in analysis because unreliable control group									

Table 4. Summary of findings*. Effects of UK Fundholding (UK)

Outcome	No of studies	Median relative eff	Quality	Comments
Drug use (number of drugs prescribed per patient)	3 [1]	Relative change: -1.6 % (-28.9 to 1.5)	Very low [2,3]	
Use of generics	2 [4]	Relative change: 15 % (-43.7 to 190.51)	Very low [2,3]	
Cost per item	2 [5]	Relative change: -44.3 % (-49.2 to -6.2)	Very low [2,3]	
Cost per patient	3 [6]	Relative change: -2.7 % (-79.7 to 66.8)	Very low [2,3]	
Total prescribing cost	1 [7]	Relative change: -50.6 % (-69.6 to -27.3)	Very low [2,3]	
Inpatient referrals	0	-	-	
Outpatient referrals	1 [8]	Adjusted relative change: -15.3 % [9]	Very low [2,3]	
*Note: presented results are ranges of results of individual studies, no meta analyses were performed				
For Footnotes see Additional table 14				

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Table 5. Summary of findings. Effects of German drug budget

Outcome	No of trials	Median relative eff	Quality	Comments
Drug use (number of drugs prescribed per patient)	1 [8]	Relative change: -13.4 %	Very low [9,10]	
Use of generics	0	-	-	
Cost per item	0	-	-	
Cost per patient	0	-	-	
Total cost	0	-	-	
Inpatient referrals	1 [11]	Relative change: 13.3 %	Very low [9,10]	
Outpatient referrals	2 [12]	Relative change: 13.2 % to -15.4 %	Very low [9,10]	
[1] There were 3 controlled interrupted time series (ITS) analyses and 5 controlled before-after (CBA) studies. Only the controlled ITS analyses are included here. The 3 controlled ITS include 3 comparisons from wave 1, and 7 comparisons from later waves				
[2] Fundholding practices were all self-selected and there is uncertainty about how comparable they are to practices that chose not to participate in fundholding				
[3] There is uncertainty about how direct the evidence, which all comes from the UK National Health Service, is for other health care systems				
[4] There were 2 controlled interrupted time				

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Table 5. Summary of findings. Effects of German drug budget (*Continued*)

series (ITS) analyses and 5 controlled before-after (CBA) studies. Only the controlled ITS analyses are included here. The 2 controlled ITS analyses include 2 comparisons from the first wave and 4 from later waves				
[5] There were 2 controlled interrupted time series (ITS) analyses and 3 controlled before-after (CBA) studies. Only the controlled ITS analyses are included here. The 2 controlled ITS analyses include 2 comparisons from the first wave and 3 from later waves				
[6] There were 3 controlled interrupted time series (ITS) analyses and 6 controlled before-after (CBA) studies. Only the controlled ITS analyses are included here. The 3 controlled ITS analyses include 3 comparisons from the first wave and 7 from later waves				
[7] 1 controlled ITS, with 3 comparisons from second and later waves				
[8] 1 CBA study that includes waves 2 and 3 in a single comparison				
[9] Long term effect (24 months), short term not reported				
[10] 1 ITS study with one outcome				

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Table 5. Summary of findings. Effects of German drug budget (*Continued*)

[11] The time series had too few data points, and the intervention was not independent of other changes since other drug policies were introduced in the same period				
[12] There is uncertainty about how direct the evidence, which all comes from Germany, is for other health care systems				
[13] 1 ITS study with one outcome				
[14] 2 ITS studies with one outcome each				

Table 6. Description of other identified budgetary policies that did not meet the inclus

Country	Policy	Motivation	Setting of budget	Setting of budget	Incentives	Disincentives	Theoretical effects
			Calculation	Negotiation partners			
New Zealand	Independent practice associations (IPA) : Umbrella organisation of GPs, specialists and other HC providers with different budgets for provided care 1993 - ?	Budgets: to increase quality of care. (IPAs: increase power of GPs towards health reforms)	IPA can choose to take a budget for diff. Services. Historical expenditure (change from FFS to Integrated capitation based budgets)	Regional health authority (or other payers) and IPA	Savings can be kept by associations to improve quality of care. Savings can be shifted between budgets	IPA's responsible for overspends, but physicians have refused to take financial responsibility	GPs within association compete for patients
USA	Managed care withholdings		Capitation minus e. g. 20%	Primary care group and HMO	Bonus if practice balance is positive	Only partial whithholding is paid in case of deficit	Keep within the budget

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Table 6. Description of other identified budgetary policies that did not meet the inclus (*Continued*)

USA	Pharmaceutical Capitation	Health plans can control the growth of their own spending by controlling the capitation levels	Target drug spending amount for a set of patients (per member per month) based on a base rate, adjusted for case mix	Providers negotiate with health pan	Later: savings will be shared by prescribers	A percentage of the difference between target and actual spending (around 70%) has to be paid by the physician	Prescribe fewer and less expensive drugs, irrespective of the capitation rate
UK	Unified budgets for new primary care groups 1999-	Accountability of GPs will help solve problems	Budget for hospital care, community health services, prescribing, infrastructure costs	Funds allocated by health authority. Compulsory for all GPs	For staff premises and computer costs. GP salary not involved		Increased monitoring needed. Since GP budget grows slower than overall budget, incentive to limit spending
Sweden	Regionalisation: responsibility of drug expenditure moved from federal to regional level 1998-	Increase the cost awareness of county councils		Government and county council	Generate savings	2002-2004: exceeding costs are covered by government, which compensates county council for up to 75% of overspent costs (ca. 9% of budget)	Development of local initiatives promoting economical prescribing (generic prescribing, drug lists etc)
Italy	Benchmarking 1980; virtual targets ("budget agreements") 1992; guidelines	Contain costs, decrease growth of drug expenditure	Local agreement (local health enterprises responsible for drug budget)	GP-association and local health enterprises	Regional savings will be distributed in terms of money or other rewards	None applied	Drugs versus overall
Spain	Regional target budgets for primary care centres and hospitals	To improve efficiency of care		Regional	About 2% of salary is dependent on prescribing targets	None (national drug budgets are always covered by in-	No abuse due to constant monitoring

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Table 6. Description of other identified budgetary policies that did not meet the inclus (*Continued*)

	2000-				(Antononaz 2002)	dustry. Physicians are paid by salary)	
Literature: New Zealand: (Willison 2002 (2)) USA: (Weiner 2000, Rosenthal 2006, Rowe 2006, Trude 2006) UK: (Whynes 1997, Klein 2004); Sweden (Lundkvist 2002; Calltorp 1996; Calltorp 1999) Italy: (Fattore 1998; Mapelli 2003; Atella 2000) Spain: (Antonanzas 2003; Lopez Bastida 2000.)							

Table 7. Effects on drug expenditures: UK Fundholding, CITS studies

				IMMEDIATE (3 months)	**SHORT TERM (6 mnths)**	**SHORT TERM (12 mnth)**	**LONG TERM (24 mnths)**
STUDY ID	STUDY ID	SETTING	ABSOLUTE LEVEL EFFECT (95% CI)	RELATIVE CHANGE (95%CI)	RELATIVE CHANGE (95%CI)	RELATIVE CHANGE (95%CI)	RELATIVE CHANGE (95%CI)
COST PER ITEM*/**							
	Rafferty*** 1997	Wave 1	-0.4 (-0.8 to 0)	-4.9 (-10.1 to 0.4)	-5.8 (-11,3 to -0,3)	-7 (-13 to -1)	-9.2 (-16.1 to -2.3)

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Table 7. Effects on drug expenditures: UK Fundholding, CITS studies (*Continued*)

	Wilson 1995***	Wave 1	-0.2 (-0.3 to -0.1)	-31.4 (-50 to -13.1)	-41.6 (-41.8 to -41.4)	-47.8 (-48.2 to -47.5)	-
	Rafferty 1997	Wave 2	-0.3 (-0.8 to 0.2)	-3.5 (-9.2 to 2.2)	-4.2 (-10.1 to 1.6)	-6.2 (-12.4 to 0)	-9.8 (-16.7 to -3)
	Wilson 1995	Wave 2	-0.2 (-0.4 to -0)	-36.9 (-71.1 to -2.7)	-45.1 (-45.5 to -44.7)	-49.2 (-49.9 to 48.5)	-
	Wilson 1995	Wave 3	-0.3 (-0.5 to -0.1)	-99.6 (-157.4 to -41.8)	-85.3 (-86 to -84.6)	-44.3 (-45.7 to 42.9)	-
COST PER PATIENT*/**							
	Rafferty 1997	Wave 1	-922.7 (-2045.8 to 200.4)	-4.9 (-10.8 to 1.1)	-4 (-10.2 to 2.3)	-7.3 (-14.2 to -0.4)	-9.1 (-17.1 to -1.1)
	Wilson 1995	Wave 1	-0 (-0.1 to 0.1)	-6 (-26.5 to 14.6)	6.7 (6.5 to 6.9)	1 (0.6 to 1.3)	-
	Harris 1996***	Wave 1	-1.2 (-3 to 0.7)	-1.2 (-3.1 to 0.7)	-0.8 (-3.3 to 1.7)	0.1 (-4 to 4.2)	2 (-5.9 to 10)
	Rafferty 1997	Wave 2	-566.6 (-1594.6 to 461.4)	-2.6 (-7.3 to 2)	-3.4 (-8.2 to 1.4)	-6.7 (-11.7 to -1.6)	-11 (-16.5 to -5.5)
	Rafferty 1997	Wave 3	-192.6 (-1482.6 to 1097.5)	-0.6 (-6 to 4.9)	-2.3 (-7.9 to 3.3)	-5.6 (-11.3 to 0.2)	n.a.
	Wilson 1995	Wave 2	-0.1 (-0.2 to -0)	-166.8 (-306.9 to -26.5)	128.6 (127.9 to 129.4)	66.8 (65.6 to 67.9)	-
	Wilson 1995	Wave 3	-0 (-0.1 to 0.1)	-1.2 (-42.4 to 39.9)	-61.5 (-61.8 to -61.2)	-79.7 (-80.2 to -79.3)	-
	Harris 1996	Wave 2	-2.9 (-4.1 to -1.7)	-2.9 (-4.1 to -1.7)	-2.8 (-4.1 to -1.4)	-2.5 (-4.1 to -0.9)	-2 (-4.3 to 0.3)

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Table 7. Effects on drug expenditures: UK Fundholding, CITS studies (*Continued*)

	Harris 1996	Wave 3	-0.6 (-2 to 0.7)	-0.6 (-2 to 0.7)	-0.6 (-2 to 0.9)	-0.5 (-2.3 to 1.4)	-0.3 (-3.4 to 2.8)
	Harris 1996	Wave 4	-1.5 (-2.9 to 0)	-1.5 (-3 to 0)	-1.9 (-3.4 to -0.5)	-2.8 (-4.5 to -1.2)	-
	Harris 1996	Wave 5	-1.2 (-2.3 to -0)	-1.2 (-2.4 to -0)	-2.1 (-3.1 to -1)	-	-
CHANGE IN TOTAL PRESCRIBING COST**							
	Harris 1996	Wave 2	-1.4 (-3.6 to 0.9)	37.6 (-24.1 to 99.3)	13.4 (-57.2 to 84.1)	-27.3 (-109.4 to 54.9)	-89.6 (-183.6 to 4.4)
	Harris 1996	Wave 3	1 (-1.5 to 3.4)	-18.8 (-65.6 to 28.4)	-35.9 (-87.6 to 15.8)	-69.6 (-127.4 to -11.9)	-97 (-160.7 to -33.3)
	Harris 1996	Wave 4	-0.3 (-3.7 to 3)	10.3 (-90.6 to 111.2)	-14.2 (-121.6 to 93.3)	-50.6 (-166.2 to 65.1)	-
	Harris 1996	Wave 5	-0.9 (-3 to 1.2)	38.7 (-50.5 to 127.9)	21.2 (-63.9 to 106.2)	-	-
*Costs of drugs dispensed from UK PACT data							
**If not otherwise noted, price year not specified in paper							
***All Rafferty outcomes: difference of mean (cost per item results for year 3 were not re-							

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Table 7. Effects on drug expenditures: UK Fundholding, CITS studies (*Continued*)

analyzable), all Harris outcomes: percentage of non-fundholders, all Wilson outcomes: difference of median							

Table 8. Effects on health care utilization (referrals): German drug budget, ITS studies

				IMMEDIATE (3 months)	**SHORT TERM (6 mnths)**	**SHORT TERM (12 mnth)**	**LONG TERM (24 mnths)**
	STUDY ID	SETTING	ABOSULUTE LEVEL EFFECT (95% CI)	RELATIVE CHANGE (95%CI)	RELATIVE CHANGE (95%CI)	RELATIVE CHANGE (95%CI)	RELATIVE CHANGE (95%CI)
REFERRALS TO OUPATIENT SPECIALISTS							
	Guether 1995	Social insurance	1543 (-5095.6 to 8181.7)	3.4 (-11.3 to 18.1)	-3.5 (-21.9 to 14.9)	-15.4 (-40.3 to 9.5)	-
	Schoeffski 1997	Social insurance	7.5 (-2 to 17)	22.8 (-6 to 51.6)	8.4 (-25 to 41.8)	13.2 (-59.3 to 85.7)	-
REFERRALS HOSPITALS							
	Schoeffski 1997	Social insurance	0.1 (0 to 0.2)	13.3 (1.2 to 25.5)	10.8 (-3.1 to 24.7)	13.3 (-16.6 to 43.2)	-

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Table 9. Effects on drug expenditures: UK Fundholding, CBA studies

			SHORT TERM	SHORT TERM (12 mnth)	LONG TERM (24 mnths)
	STUDY ID	SETTING	ADJUSTED ABSOLUTE CHANGE	ADJUSTED RELATIVE CHANGE [%]	ADJUSTED RELATIVE CHANGE [%]
COST PER ITEM					
	Bradlow 1993	Wave 1	-0.5	-6.3	
	Rafferty 1997	Wave 1	-0.4	-5.5	-8.1
	Bradlow 1993	Wave 1	-	-	-5.2*/***
	Wilson 1995	Wave 1	-	-	-0.9*
	Rafferty 1997	Wave 2	-0.5	-5.3	-9.9
	Rafferty 1997	Wave 3	-0.5	-5.3	n.a.
	Wilson 1995	Wave 2	-	-	0,3*
	Wilson 1995	Wave 3	-	-	-0.3*
	Wilson 1999	Wave 3/4	-	-	-2.8**
COST PER ITEM PPIs					
	Wilson 1999	Wave 3/4	-	-	-1**
COST PER ITEM SSRIs					
	Wilson 1999	Wave 3/4	-	-1.9	-2.7**
COST PER PATIENT					
	Rafferty 1997	Wave 1	-8.4	-9.5	-15.3
	Burr 1992	Wave 1	-0.6	-4.5	-
	Harris 1996	Wave 1	-1.2	-3.2	-7.7
	Wilson 1995	Wave 1	-	-	-7.9*
	Bradlow 1993	Wave 1	-0.8	-4.6	-

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Table 9. Effects on drug expenditures: UK Fundholding, CBA studies (*Continued*)

	Bradlow 1993	Wave 1	-1.1	-6.2	0.4*/***
	Rafferty 1997	Wave 2	-7.2	-7.2	-13.9
	Rafferty 1997	Wave 3	-7.7	-7	-
	Baines 1997 Lincolns	Wave 1-3	-	-	-18.5*
	Baines 1997 Devon	Wave 1-3	-	-	-16.4*
	Whynes 1997	Wave 4	-0.7	-	-
	Corney 1997	Wave 2	0.2	0.5	-4.8
	Harris 1996	Wave 2	-1.7	-4	-6.4
	Wilson 1995	Wave 2	-	-	-7.1*
	Harris 1996	Wave 3	-1.8	-3.7	-4.4
	Wilson 1995	Wave 3	-	-	-2.7*
	Harris 1996	Wave 4	-1.8	-3.4	-5.6
	Harris 1996	Wave 5	-1.9	-3.4	-
COST PER PATIENT ALL ANTI-ULCER DRUGS					
	Wilson 1999	Wave 3/4	-	-	-10.6**
COST PER PATIENT ALL ANTI-DEPRESSANT DRUGS					
	Wilson 1999	Wave 3/4	-	-	-1.9**
All costs in Brit. £, if not noted otherwise, price year not specified					
*3 year f/u					

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Table 9. Effects on drug expenditures: UK Fundholding, CBA studies (*Continued*)

**Combined wave 4: 1year f/u, wave 3: 2 year f/u						
***Data from Stewart Brown study						

Table 10. Effects on drug use: UK Fundholding, CITS studies

ITEMS PER PATIENT				**IMMEDIATE (3 months)**	**SHORT TERM (6 mnths)**	**SHORT TERM (12 mnth)**	**LONG TERM (24 mnths)**
	STUDY ID	SETTING	ABOSULUTE LEVEL EFFECT (95% CI)	RELATIVE CHANGE (95%CI)	RELATIVE CHANGE (95%CI)	RELATIVE CHANGE (95%CI)	RELATIVE CHANGE (95%CI)
	Rafferty 1997	Wave 1	-63.6 (-249.3 to 122.1)	-2.5 (-9.8 to 4.9)	-1 (-8.8 to 6.8)	-2.8 (-11.5 to 5.9)	0.2 (-10.3 to 10.7)
	Harris 1996	Wave 1	0.4 (-1.1 to 1.8)	0.4 (-1.2 to 2)	0.7 (-1.3 to 2.7)	1.4 (-1.5 to 4.2)	2.6 (-2.1 to 7.2)
	Wilson 1995	Wave 1	1.4 (-6.6 to 9.4)	1.9 (-9.3 to 13.1)	-4.1 (4.3 to -4)	-10.2 (-10.4 to -10)	-
	Rafferty 1997	Wave 2	-43.6 (-257 to 169.8)	-1.6 (-9.2 to 6)	-2.4 (-10.3 to 5.5)	-3.6 (-12.1 to 4.8)	-4.2 (-13.7 to 5.4)
	Rafferty 1997	Wave 3	-44.3 (-280.1 to 191.4)	-1.4 (-9.9 to 7)	1.5 (-7.2 to 10.1)	1.5 (-7.5 to 10.5)	-
	Wilson 1995	Wave 2	2.7 (-9.5 to 14.9)	7.1 (-25.1 to 39.2)	-15.8 (-16.1 to -15.5)	-14.5 (-15.2 to -13.9)	-
	Wilson 1995	Wave 3	4.8 (-4.8 to 14.4)	16.8 (-17.1 to 50.8)	-21.3 (-21.6 to -20.9)	-28.9 (-29.4 to -28.3)	-
	Harris 1996	Wave 2	-0.5 (-1.3 to 0.3)	-0.5 (-1.3 to 0.3)	-0.4 (-1.3 to 0.5)	-0.3 (-1.4 to 0.8)	-0.1 (-1.7 to 1.5)

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Table 10. Effects on drug use: UK Fundholding, CITS studies (*Continued*)

	Harris 1996	Wave 3	0.0 (-0.7 to 0.7)	0.0 (-0.8 to 0.8)	0.0 (-0.8 to 0.9)	0.2 (-0.7 to 1.2)	0.4 (-0.7 to 1.6)
	Harris 1996	Wave 4	0.3 (-0.4 to 1)	0.3 (-0.4 to 1.1)	0.1 (-0.6 to 0.9)	-0.4 (-1.2 to 0.5)	-
	Harris 1996	Wave 5	-0.2 (-1 to 0.5)	-0.2 (-1 to 0.5)	-0.2 (-1 to 0.6)	-	-
GENERIC PERCENTAGE							
	Rafferty 1997	Wave 1	2.8 (1.5 to 4.1)	10.8 (5.6 to 16)	12.7 (7.1 to 18.2)	15.8 (9.4 to 22.2)	23 (15 to 31)
	Wilson 1995	Wave 1	1.7 (0.8 to 2.7)	345.7 (151.8 to 539.6)	342.7 (341.1 to 344.4)	190.5 (189 to 192)	-
	Rafferty 1997	Wave 2	1.3 (-0.2 to 2.9)	5.1 (-0.9 to 11.1)	5.9 (-0.4 to 12.2)	8.5 (1.6 to 15.5)	13.6 (5.4 to 21.7)
	Rafferty 1997	Wave 3	0.5 (-1 to 1.9)	1.8 (-3.9 to 7.4)	5.7 (-0.1 to 11.5)	14.2 (8.1 to 20.4)	-
	Wilson 1995	Wave 2	1.0 (-0.1 to 2.1)	45.4 (-2.4 to 93.2)	66.5 (66.1 to 66.8)	68.1 (67.6 to 68.7)	-
	Wilson 1995	Wave 3	1.9 (0.8 to 3)	35.5 (15.1 to 55.9)	-12.2 (-12.4 to -12.1)	-43.7 (-43.5 to -44.0)	-

Table 11. Effects on drug use: UK Fundholding, CBA studies

			SHORT TERM	**SHORT TERM (12 mnth)**	**LONG TERM (24 mnths)**
	STUDY ID	SETTING	ADJUSTED ABSOLUTE CHANGE	ADJUSTED RELATIVE CHANGE [%]	ADJUSTED RELATIVE CHANGE [%]
ITEMS PER PATIENT					
	Burr 1992	Wave 1	18	0.8	-
	Rafferty 1997	Wave 1	-461	-4	-5.2

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Table 11. Effects on drug use: UK Fundholding, CBA studies (*Continued*)

	Bradlow 1993	Wave 1	40	1.8	-
	Bradlow 1993	Wave 1	-	-	3,6**/****
	Wilson 1995**	Wave 1	-	-5.7*	-
	Rafferty 1997	Wave 2	-218	-1.8	-2.6
	Rafferty 1997	Wave 3	-211	-1.7	-
	Wilson 1995*	Wave 2	-	-	0.8**
	Wilson 1995*	Wave 3	-	-	-5.6**
	Wilson 1999	Wave 3/4	-	-	39.2***
	Whynes 1997	Wave 4	-	-1.2	-
GENERIC PERCENTAGE					
	Rafferty 1997	Wave 1	3.2	12.7	16.1
	Bradlow 1993	Wave 1	4.1	8.8	-
	Bradlow 1993	Wave 1	-	-	17.2**/****
	Wilson 1995	Wave 1	-	-	12.1**
	Rafferty 1997	Wave 2	2.4	9.5	13.6
	Wilson 1995	Wave 2	-	-	10,1**
	Rafferty 1997	Wave 3	3.4	13.4	-
	Wilson 1995	Wave 3	-	-	10.3**
	Baines 1997 Lincolns.	Wave 1-3	-	-	10.7**
	Baines 1997 Devon	Wave 1-3	-	-	9.5**
	Whynes 1997	Wave 4	3.5	-	-
	Wilson 1999*	Wave 3/4	-	-	4***
ALL ANTI-ULCER DRUGS (DDD)					

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Table 11. Effects on drug use: UK Fundholding, CBA studies (*Continued*)

	Wilson 1999	Wave 3/4	-	-	-6.7***
PERCENTAGE PPI OF ALL ANTI-ULCER DRUGS (DDD)					
	Wilson 1999	Wave 3/4	-	-	-7.9***
ALL ANTI-DEPRESSANT DRUGS (DDD)					
	Wilson 1999	Wave 3/4	-	-	-7.9***
PERCENTAGE SS-RIs OF ALL ANTI-DEPRESSANT DRUGS [DDD]					
	Wilson 1999	Wave 3/4	-	-	-0.8***
*Median					
**3 year f/u					
***Combined wave 4: 1year f/u, wave 3: 2 year f/u					
****Data from Stewart-Brown study					

Table 12. Effects on health care utilization (referrals): UK Fundholding, CBA studies

			LONG TERM	**SHORT TERM (12 mnth)**	**LONG TERM (24 mnths)**
	STUDY ID	SETTING	ADJUSTED ABSOLUTE CHANGE	ADJUSTED RELATIVE CHANGE [%]	ADJUSTED RELATIVE CHANGE [%]
REFERRALS TO NHS OUTPATIENT CARE					

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Table 12. Effects on health care utilization (referrals): UK Fundholding, CBA studies (*Continued*)

	Kammerling 1996	Wave 2/3	-18.9	-	-15.3

Table 13. Effects on drug expenditures: Ireland Indicative budgets (IDTSS), ITS studies

				IMMEDIATE (3 months)	**SHORT TERM (6 mnths)**	**SHORT TERM (12 mnth)**	**LONG TERM (24 mnths)**
	STUDY ID	SETTING	ABOSU-LUTE LEVEL EFFECT (95% CI)	RELATIVE CHANGE (95%CI)	RELATIVE CHANGE (95%CI)	RELATIVE CHANGE (95%CI)	RELATIVE CHANGE (95%CI)
COST PER ITEM*							
	Walley 2000	IDTSS	0.1 (-2.5 to 2.8)	-	-	0.6 (-10.1 to 11.7)	1.2 (-12.9 to 15.3)
TOTAL PRE-SCRIBING COST**							
	Walley 2000	IDTSS	-5.2 (-10 to -0.4)	-	-	-18.0 (-34.6 to -1.4)	-21.7 (-41.7 to -1.8)
*If not oth-erwise noted, price year not spec-ified in paper							

Table 14. Effects on drug use: Ireland Indicative budgets (IDTSS), ITS studies

				IMMEDIATE (3 months)	**SHORT TERM (6 mnths)**	**SHORT TERM (12 mnth)**	**LONG TERM (24 mnths)**
	STUDY ID	SETTING	ABOSU-LUTE LEVEL EFFECT (95% CI)	RELATIVE CHANGE (95%CI)	RELATIVE CHANGE (95%CI)	RELATIVE CHANGE (95%CI)	RELATIVE CHANGE (95%CI)
ITEMS PER PATIENT							

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Table 14. Effects on drug use: Ireland Indicative budgets (IDTSS), ITS studies (*Continued*)

	Walley 2000	IDTSS	-0.8 (-1.4 to -0.2)		-	-8.2 (-14.4 to -2.0)	-10.1 (-17.5 to -2.7)

Table 15. Effects on drug use: German drug budget, ITS studies

				IMMEDIATE (3 months)	**SHORT TERM (6 mnths)**	**SHORT TERM (12 mnth)**	**LONG TERM (24 mnths)**
	STUDY ID	SETTING	ABOSULUTE LEVEL EFFECT (95% CI)	RELATIVE CHANGE (95%CI)	RELATIVE CHANGE (95%CI)	RELATIVE CHANGE (95%CI)	RELATIVE CHANGE (95%CI)
ITEMS PER PATIENT							
	Guether 1995	Social insurance	-34552 (-99896 to 30791)	-11.2 (-32.3 to 10.0)	-12.1 (-37.8 to 13.7)	-13.4 (-48.9 to 22.1)	n.a

Table 16. Factors that could modify the effects of drug budgets

FACTOR	**DESCRIPTION**	**POTENTIAL EFFECTS OF**
Budget (target) level	Level of set budget should offer room for improvement but be reachable	If too high or too low: Drug use: Less shift towards cheaper drugs Drug expenditure: Less decrease Health care utilisation: Setting dependent Patient drug expenditures: Setting dependent
Budget strictness / directness	- Virtual budgets / agreement without consequences - Collective budgets - Individual budgets	The more direct the effect for the individual prescriber, the stronger the effects
Incentives / disincentives	- Only savings can be achieved - only punishments - both	
Services covered under the budget	If only prescribing costs are subject to a budget, costs might be shifted to other sectors of care	Drug use: Decrease Referrals: Increase if not covered in budget Health: Decrease if care is delayed, increased if more specialist care or shorter waiting time

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Table 16. Factors that could modify the effects of drug budgets (*Continued*)

		Health care utilisation: Increase
Available feedback information	Should be available to prescribers in order to react	Drug use: Less shift towards cheaper drugs or overreaction Drug expenditure: Less decrease Health: Potential for under-treatment
Concurrent policy changes: "Co-payment changes "Reference pricing "Negative lists etc	Should not be introduced simultaneously if individual effects should be assessed	Drug use: Unclear Health: Unclear Health care utilisation: Unclear
Gatekeeping, patient lists	If primary care physician acts as gatekeeper and patients have a limited choice of care provider, physicians might be less dependent on patients preferences	Drug use: Less shift towards cheaper drugs Drug expenditure: Less decrease Health: Unclear Health care utilisation: Increase
Practice characteristics	- Practice size - Level of organization, efficiency - number of partners	Drug use: Less shift towards cheaper drugs Health: Decrease Health care utilisation: Increase Patient drug expenditures: Increased
Dispensing practices	Practice can dispense medicines	Drug use: Bigger shift towards cheaper drugs Drug expenditure: Stronger decrease

APPENDICES

Appendix 1. Search strategies: MEDLINE OVID

The MEDLINE Ovid search strategy used both MeSH terms and text words (tw):
1. *Physician's Practice Patterns/ 2. *Group Practice/ 3. *Institutional Practice/ 4. *Partnership Practice/ 5. *Private Practice/ 6. *Family Practice/ 7. *Physicians/ 8. *Physicians, Family/

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(*Continued*)

9. *Professional Practice/
10. *Nurses/
11. *Nurse Clinicians/
12. *Nurse Practitioners/
13. *Pharmacists/
14. *Pharmacies/
15. *Pharmacy/
16. *Hospitals/
17. (physician$ or GP? or doctor? or prescriber? or group pract$ or institutional pract$ or partnership pract$ or family pract$ or general pract$ or office pract$ or private pract$ or primary pract$ or nurse or nurses).tw.
18. (pharmacist? or pharmacies or pharmacy).tw.
19. hospital?.tw.
20. or/1-19
21. *Drug Information Services/
22. *Pharmacists/
23. *Community Pharmacy Services/
24. *Reminder Systems/
25. *Feedback/
26. *Education, Continuing/
27. *Education, Medical, Continuing/
28. *Education, Nursing, Continuing/
29. *Education, Pharmacy, Continuing/
30. *Guidelines/
31. *Practice Guidelines/
32. *Guideline Adherence/
33. *Budgets/
34. *Motivation/
35. *Physician Incentive Plans/
36. *Capitation Fee/
37. *Reimbursement, Incentive/
38. *Income/
39. *"Salaries and Fringe Benefits"/
40. *Benchmarking/
41. *Drug Monitoring/
42. *Adverse Drug Reaction Reporting Systems/
43. *Product Surveillance, Postmarketing/
44. drug information.tw.
45. pharmacist?.tw.
46. reminder?.tw.
47. feedback.tw.
48. (continuing adj1 education).tw.
49. (guideline? adj1 (disseminat$ or implement$ or compliance or adherence or distribut$)).tw.
50. ((drug? or pharmaceutic$ or prescrib$ or prescrip$) adj1 budget?).tw.
51. (incentive? adj1 (plan? or money$ or financ$ or payment? or reimburs$)).tw.
52. capitation.tw.
53. (salaries or salary or income? or wages or fringe benefit?).tw.
54. benchmarking.tw.
55. ((review or report$ or monitor$ or surveillance or evaluat$) adj1 (drug use? or drug utilization or drug utilisation or prescrib$ or prescrip$)).tw.

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(*Continued*)

56. outreach.tw.
57. visit?.tw.
58. (letter? or mail$).tw.
59. (telephon$ or phon$).tw.
60. ((academic or group) adj1 detailing).tw.
61. fundhold$.tw.
62. ((prescrib$ or prescrip$) adj1 scheme?).tw.
63. or/21-62
64. *Prescriptions, Drug/
65. *Drug Utilization/
66. *"Drug Utilization Review"/
67. ((prescrib$ or prescrip$) adj2 (attitude or variation? or behavior or behaviour or pattern? or practice? or habit? or accurate or trend? or cost? or effect? or change? or shift$ or rational or reduc$ or improv$ or influenc$ or expenditure? or rate? or data)).tw.
68. (drug use? or drug utilizarion or drug utilisation).tw.
69. or/64-68
70. random$.tw.
71. multicenter study.pt.
72. randomized controlled trial.pt.
73. controlled clinical trial.pt.
74. clinical trial.pt.
75. intervention studies/
76. experiment$.tw.
77. (time adj series).tw.
78. (pre test or pretest or (posttest or post test)).tw.
79. random allocation/
80. impact.tw.
81. intervention?.tw.
82. chang$.tw.
83. evaluation studies/
84. evaluat$.tw.
85. effect?.tw.
86. comparative studies/
87. compar$.tw.
88. or/70-87
89. editorial.pt.
90. letter.pt.
91. comment.pt.
92. or/89-91
93. animals/
94. humans/
95. 93 not 94
96. 92 or 95
97. 20 and 63 and 69 and 88
98. 97 not 96

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Appendix 2. Search strategies: EMBASE

EMBASE Ovid
Search fields: A combination of EMTAGS and text words
1. Clinical Practice/
2. General Practice/
3. Medical Practice/
4. Private Practice/
5. Professional Practice/
6. Group Practice/
7. General Practitioner/
8. Physician/
9. Nurse/
10. Nurse Practitioner/
11. Pharmacist/
12. Pharmacy/
13. Hospital Pharmacy/
14. Clinical Pharmacy/
15. Hospital/
16. (physician$ or GP? or doctor? or prescriber? or group pract$ or institutional pract$ or partnership pract$ or family pract$ or general pract$ or office pract$ or private pract$ or primary pract$ or nurse or nurses).tw.
17. (pharmacist? or pharmacies or pharmacy).tw.
18. hospital?.tw.
19. or/1-18
20. *Drug Information/
21. *Pharmacist/
22. *Reminder System/
23. *Feedback System/
24. *Continuing Education/
25. *Medical Education/
26. *Education/
27. *Nursing Education/
28. *Practice guideline/
29. *Budget/
30. *Motivation/
31. *Capitation Fee/
32. *Medical Fee/
33. *Income/
34. *Physician Income/
35. *Salary/
36. *Drug Monitoring/
37. *Postmarketing surveillance/
38. *Drug Surveillance Program/
39. drug information.tw.
40. pharmacist?.tw.
41. reminder?.tw.
42. feedback.tw.
43. (continuing adj1 education).tw.

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(*Continued*)

44. (guideline? adj1 (disseminat$ or implement$ or compliance or adherence or distribut$)).tw.
45. ((drug? or pharmaceutic$ or prescrib$ or prescrip$) adj1 budget?).tw.
46. (incentive? adj1 (plan? or money$ or financ$ or payment? or reimburs$)).tw.
47. capitation.tw.
48. (salaries or salary or income? or wages or fringe benefit?).tw.
49. benchmarking.tw.
50. ((review or report$ or monitor$ or surveillance or evaluat$) adj1 (drug use? or drug utilization or drug utilisation or prescrib$ or prescrip$)).tw.
51. outreach.tw.
52. visit?.tw.
53. (letter? or mail$).tw.
54. (telephon$ or phon$).tw.
55. ((academic or group) adj1 detailing).tw.
56. fundhold$.tw.
57. ((prescrib$ or prescrip$) adj1 scheme?).tw.
58. or/20-57
59. *Prescription/
60. *"Drug Use"/
61. *Drug Utilization/
62. ((prescrib$ or prescrip$) adj2 (attitude or variation? or behavior or behaviour or pattern? or practice? or habit? or accurate or trend? or cost? or effect? or change? or shift$ or rational or reduc$ or improv$ or influenc$ or expenditure? or rate? or data)).tw.
63. (drug use? or drug utilization or drug utilisation).tw.
64. or/59-63
65. randomized controlled trial/
66. random$.tw.
67. experiment$.tw.
68. (time adj series).tw.
69. (pre test or pretest or post test or posttest).tw.
70. impact.tw.
71. intervention?.tw.
72. chang$.tw.
73. evaluat$.tw.
74. effect$.tw.
75. compar$.tw.
76. or/65-75
77. letter.pt.
78. editorial.pt.
79. nonhuman/
80. or/77-79
81. 19 and 58 and 64 and 76
82. 81 not 80

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Appendix 3. Search strategies: Effective Practice and Organisation of Care Group Register

Effective Practice and Organisation of Care Group Register, Idealist database
Searched terms anywhere in text
drug [or] drugs [or] pharmaceutic* [or] medicines [or] medicat* [or] prescrip* [or] prescrib*

Appendix 4. Search strategies: CENTRAL

CENTRAL, The Cochrane Central Register of Controlled Trials, Ovid
Search fields: A combination of MeSH terms and text words

1. (regulat$ or requirement? or restrict$ or monitor$ or control$).tw.
2. (legislation? or law? or act? or policy or policies or politics or reform$ or system? or plan$ or program$ or strateg$).tw. or Policy Making/ or Legislation, Drug/ or Public Policy/ or Health Policy/ or Politics/ or Health Care Reform/
3. (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$).tw. or exp Pharmaceutical Preparation/ or Drug Utilization/
4. (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$).tw. or exp Pharmaceutical Preparation/ or Drug Industry/ or Drug Utilization/
5. (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$).tw. or exp Pharmaceutical Preparation/ or Prescriptions, Drug/ or Drug Utilization/
6. Drug Approval/ or (approv$ adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
7. Licensure/ and 4
8. Drug Labeling/
9. ((licens$ or registrat$ or label$) adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
10. (6 or 7 or 8 or 9) and (1 or 2)
11. Classification/ and 3 and 2
12. ((classify$ or classification?) adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw. and 2
13. 11 or 12
14. 10 or 13
15. Patents/ and 4
16. (patent? adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
17. ((profit$ adj3 (control$ or reduc$ or regulat$ or fix$ or restrict$)) and (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
18. (15 or 16 or 17) and (1 or 2)
19. (Marketing/ or Marketing of Health Services/ or Advertising/) and 4
20. ((advert$ or promot$ or market$) adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
21. (19 or 20) and (1 or 2)
22. (Insurance, Hospitalization/ or Insurance, health, reimbursement/ or Reimbursement Mechanisms/ or Reimbursement, disproportionate share/ or Reimbursement, incentive/) and 5
23. Insurance, pharmaceutical services/
24. ((reimburse$ or insur$ or (third party adj1 pay$) or benefit plan?) adj3 (drug or drugs or pharmaceutic$ or pharmacy or pharmacies or medicines or medicament? or medicat$)).tw.
25. (22 or 23 or 24) and (1 or 2)

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(*Continued)*

26. Formularies/ and 5
27. Formularies, Hospital/ and 3
28. ((formulary or formularies or positive list? or negative list?) adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$ or hospital?)).tw.
29. (26 or 27 or 28) and (1 or 2)
30. Drugs, Essential/
31. (essential adj3 (drug? or pharmaceutic$ or medicine? or medicament?)).tw.
32. ((drug? or pharmaceutic$ or medicine? or medicament?) adj3 list?).tw.
33. 31 and 32
34. 30 or 33
35. ((pre-authori#ation? or preauthori#ation? or prior authori#ation?) adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
36. Reminder Systems/ and 5 and 2
37. (reminder? adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw. and 2
38. Prescriptions, Drug/
39. (continu$ adj3 education).tw.
40. Education, Continuing/
41. Education, Pharmacy, Continuing/
42. (improv$ or incentive?).tw.
43. 39 or 40 or 41 or 42
44. 38 and 43 and (1 or 2)
45. (((prescrib$ or prescription?) adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)) and ((continu$ adj1 education) or (improv$ or incentive?))).tw. and (1 or 2)
46. (Guidelines/ or Practice Guidelines/ or Guideline Adherence/) and 2 and 5
47. (((guideline? or recommendation?) adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)) and (disseminat$ or implement$ or complian$ or adherence)).tw. and 2
48. 46 or 47
49. (((generic$ adj3 prescrib$) or (generic$ adj3 prescription?)) adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
50. ((local$ or global$) adj3 budget$).tw.
51. (budget$ adj3 (general pract$ or GP? or physician? or doctor?)).tw.
52. 50 and 51
53. (fundhold$ adj3 (general pract$ or GP? or physician? or doctor?)).tw.
54. 52 or 53
55. 54 and 3
56. "Pharmacy and Therapeutics Committee"/ and 2 and 5
57. ((drug? or formulary or pharmac$) adj3 committee?).tw. and 2
58. 56 or 57
59. (Drug Monitoring/ or Adverse Drug Reaction Reporting Systems/ or (safe$ adj1 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.) and 2
60. Product Surveillance, Postmarketing/ and 3 and 2
61. 59 or 60
62. 36 or 37 or 44 or 45 or 48 or 49 or 55 or 58 or 61
63. (Cost Control/ or Cost Savings/) and 5 and 2
64. ((control$ or containment or curtailment or reduc$ or save or saving) adj3 cost?).tw.
65. (cost? adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
66. 64 and 65 and 2
67. ((control$ or reduc$ or cut$ or regulat$ or negotiat$ or fix$) adj3 (price? or pricing)).tw.
68. ((price? or pricing) adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.

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(*Continued)*

69. 67 and 68 and 2
70. (reference$ adj3 (price? or pricing)).tw.
71. ((price? or pricing) adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
72. 70 and 71
73. (index$ adj3 (price? or pricing)).tw.
74. ((price? or pricing) adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
75. 73 and 74
76. (maxim$ adj3 (price? or pricing)).tw.
77. ((price? or pricing) adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
78. 76 and 77
79. (cost? effect$ adj3 (price? or pricing)).tw.
80. ((price? or pricing) adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
81. 79 and 80
82. (reimbursement contract? adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
83. (Drug Cost/ or Economics, Pharmaceutical/) and (1 or 2)
84. (Purchasing, Hospital/ or Group, Purchasing/) and 3
85. (purchas$ adj3 (group? or join$ or hospital? or shared)).tw.
86. ((group? or join$ or hospital? or shared) adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
87. 85 and 86 and 2
88. (procurement$ adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw. and 2
89. (rebate? adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw. and 2
90. 63 or 66 or 69 or 72 or 75 or 78 or 81 or 82 or 83 or 84 or 87 or 88 or 89
91. Marketing/ or Marketing of Health Services/ or Advertising/ or Licensure/ or Drug Labeling/
92. Pharmacies/ or Pharmacists/ or (pharmacy or pharmacies or pharmacist? or retailer? or wholesaler? or supplier? or dispens$).tw.
93. 91 and 92 and 3 and (1 or 2)
94. (advert$ or promot$ or market$).tw.
95. Pharmacies/ or Pharmacists/ or (pharmacy or pharmacies or pharmacist? or retailer? or wholesaler? or supplier? or dispens$).tw.
96. 94 and 95 and 3 and (1 or 2)
97. 93 or 96
98. ((control$ or reduc$ or regulat$ or fix$ or restrict$) adj3 profit?).tw.
99. (profit? adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
100. Pharmacies/ or Pharmacists/ or (pharmacy or pharmacies or pharmacist? or retailer? or wholesaler? or supplier? or dispens$).tw.
101. 98 and 99 and 100
102. (generic$ adj3 substitut$).tw.
103. (substitut$ adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
104. 102 and 103
105. (licens$ adj3 (pharmacy or pharmacies)).tw.
106. (((supply or supplies or distribut$ or sale$) adj3 (drug or drugs or pharmaceutic$ or medicines or medicament$ or medicat$)) and (pharmacy or pharmacies or retailer? or wholesaler? or supplier? or dispens$)).tw. and (1 or 2)
107. 97 or 101 or 104 or 105 or 106
108. Cost Sharing/ and 5
109. (cost? adj3 (sharing or share)).tw.
110. ((sharing or share) adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
111. 109 and 110
112. (out of pocket? adj3 pay$).tw.
113. (pay$ adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
114. 112 and 113
115. ((copay$ or co pay$) adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
116. ((prescrib$ or prescription? or pharmaceutic$ or pharmacy or pharmacies or dispens$) adj3 (charg$ or fee?)).tw.

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(*Continued*)

117. ((charg$ or fee?) adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
118. 116 and 117
119. ((prescrib$ or prescription?) adj3 (limit$ or cap$)).tw.
120. ((limit$ or cap$) adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
121. 119 and 120
122. ((coinsurance or deductible?) adj3 (drug or drugs or pharmaceutic$ or medicines or medicament$ or medicat$)).tw.
123. "Deductibles and Coinsurance"/ and 5
124. Fees, Pharmaceutical/
125. Prescription Fees/
126. Capitation Fee/ and 5
127. 108 or 111 or 114 or 115 or 118 or 121 or 122 or 123 or 124 or 125 or 126
128. Drug Information Services/ and (patient? or consumer?).tw. and 2
129. Drug Labeling/ and (patient? or consumer?).tw. and 2
130. Patient Education/ and 3 and (1 or 2)
131. ((educat$ or inform$) adj3 (patient? or consumer?)).tw.
132. ((patient? or consumer?) adj3 (drug or drugs or pharmaceutic$ or medicines or medicament? or medicat$)).tw.
133. 131 and 132 and (1 or 2)
134. 128 or 129 or 130 or 133
135. 14 or 18 or 21 or 25 or 29 or 34 or 35 or 62 or 90 or 107 or 127 or 134

Appendix 5. Search strategies: CSA Worldwide Political Science Abstracts

CSA Worldwide Political Science Abstracts Search field: 'Key Words'
KW=(legislation OR law* OR act* OR policy OR policies OR politics OR reform* OR system* OR plan* program* OR strateg* OR regulat* OR requirement* OR restrict* OR monitor* OR control) AND KW=(drug* OR pharmaceutic* OR medicines OR medicament* OR medicat*) AND KW=(random* OR intervention* OR control* OR compar* OR evaluat* OR time OR longitud* OR repeated measure* OR pretest OR posttest OR pre test OR post test OR impact* OR chang* OR effect* OR experiment*)

Appendix 6. Search strategies: EconLit

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EconLit, WebSPIRS
Search filed: 'Terms Anywhere'
regulat* or requirement or restrict* or monitor* or control* or legislation or law? or act? or policy or policies or politics or reform* or system? or plan* or program? or strateg*)
and
(drug? or pharmaceutic* or medicines or medicament? or medicat*)
and
(random* or intervention? or control* or compar* or evaluat* or time or pretest or posttest or pre test or post test or impact? or chang* or effect? or experiment?)

Appendix 7. Search strategies: SIGLE

SIGLE, System for Information on Grey Literature in Europe, WebSPIRS
Search field: 'Terms Anywhere'
(regulat* or requirement or restrict* or monitor* or control* or legislation or law? or act? or policy or policies or politics or reform* or system? or plan* or program? or strateg*)
and
(drug? or pharmaceutic* or medicines or medicament? or medicat*)
and
(random* or intervention? or control* or compar* or evaluat* or time or pretest or posttest or pre test or post test or impact? or chang* or effect? or experiment?)

Appendix 8. Search strategies: INRUD

INRUD, International Network for Rational Use of Drugs
Search field: 'All non-indexed fields'
{drug} or {pharmaceutic} or {medicines} or {medicament} or {medicat}
AND
{regulat} or {requirement} or {restrict} or {monitor} or {control} or {legislation} or {law} or {act} or {policy} or {policies} or {politics} or {reform} or {system} or {plan} or {program} or {strateg}
AND
{random} or {intervention} or {control} or {compar} or {evaluat} or {time} or {pretest} or {posttest} or {pre test} or {post test} or {impact} or {chang} or {effect} or {experiment}

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Appendix 9. Search strategies: PAIS International

PAIS International, Public Affairs Information Service, WebSPIRS
Search fields: 'Descriptors' or 'Title' or 'Abstract'
1.((explode "Drug-stores" in DE) or (explode "Pharmacists" in DE) or (explode "Prescriptions" in DE) or (explode "Drugs" in DE) or (explode "Pharmaceutical-industry" in DE)
OR
((((drug? or pharmaceutic* or medicines or medicament? or medicat*)) in AB)
OR
(((drug? or pharmaceutic* or medicines or medicament? or medicat*)) in TI)))
AND
((((random* or intervention? or control* or compar* or evaluat* or time or pretest or posttest or pre test or post test or impact? or chang* or effect? or experiment?)) in AB)
OR
(((random* or intervention? or control* or compar* or evaluat* or time or pretest or posttest or pre test or post test or impact? or chang* or effect? or experiment?)) in TI))
AND
((((regulat* or requirement or restrict* or monitor* or control* or legislation or law? or act? or policy or policies or politics or reform* or system? or plan* or program? or strateg*)) in AB)
OR
(((regulat* or requirement or restrict* or monitor* or control* or legislation or law? or act? or policy or policies or politics or reform* or system? or plan* or program? or strateg*)) in TI))
2.((narco* or crim* or war? or terror* or weapon? or addict* or abus* or traffic* or illicit*) in AB)
OR
((narco* or crim* or war? or terror* or weapon? or addict* or abus* or traffic* or illicit*) in TI)
3. (1 AND 2) NOT 3

Appendix 10. Search strategies: International Political Science Abstracts

International Political Science Abstracts, WebSPIRS
Search field: 'Terms Anywhere'
(regulat* or requirement or restrict* or monitor* or control* or legislation or law? or act? or policy or policies or politics or reform* or system? or plan* or program? or strateg*)
and
(drug? or pharmaceutic* or medicines or medicament? or medicat*)
and
(random* or intervention? or control* or compar* or evaluat* or time or pretest or posttest or pre test or post test or impact? or chang* or effect? or experiment?)

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Appendix 11. Search strategies: NHS EED

NHS EED, National Health Services Economic Evaluation Database, CRD
Search fields: A combination of 'Subject Headings' and 'All fields'
Search done in 6 separate stages
1.drug-approval or licensure or drug-labeling or classification or patents or marketing or marketing-of-health-services or advertising/ Subject Headings
AND
drug or pharmac or medicin or medica or prescri/All fields
AND
regulat or require or restrict or monitor or control or legislation or law or act or policy or policies or politics or reform or system or plan or program or strateg/All fields
2.insurance-hospitalization or insurance-health-reimbursement or reimbursement- mechanisms or reimbursement-disproportionate-share or reimbursement-incentive or insurance-pharmaceutical-services/Subject Headings
AND
drug or pharmac or medicin or medica or prescri/All fields
AND
regulat or require or restrict or monitor or control or legislation or law or act or policy or policies or politics or reform or system or plan or program or strateg/All fields
3.formularies or formularies-hospital or drugs-essential or reminder-systems or prescriptions-drug or education-continuing or education-pharmacy-continuing or guidelines or practice-guidelines or guideline-adherence/Subject Headings
AND
drug or pharmac or medicin or medica or prescri/All fields
AND
regulat or require or restrict or monitor or control or legislation or law or act or policy or policies or politics or reform or system or plan or program or strateg/All fields
4.drug-monitoring or adverse-drug-reaction-reporting-systems or product-surveillance-postmarketing/Subject Headings
AND
drug or pharmac or medicin or medica or prescri/All fields
AND
regulat or require or restrict or monitor or control or legislation or law or act or policy or policies or politics or reform or system or plan or program or strateg/All fields
5.deductibles or coinsurance or fees-pharmaceutical or prescription-fees or capitation-fee or drug-information-services or patient-education /Subject Headings
AND
drug or pharmac or medicin or medica or prescri/All fields
6.cost-control or cost savings or drug-cost or economics-pharmaceutical or purchasing-hospital or group-purchasing or pharmacies or pharmacists or cost-sharing/Subject Headings
AND
drug or pharmac or medicin or medica or prescri/All fields
AND
regulat or require or restrict or monitor or control or legislation or law or act or policy or policies or politics or reform or system or plan or program or strateg/All fields

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Appendix 12. Search strategies: NTIS

NTIS, National Technical Information service
Search fields: A combination of 'Index Terms' (KT), 'Key Words/Phrases' (no tag) and 'Title'
#1. KT=PHARMACEUTICALS OR KT=DRUGS OR KT=MEDICATIONS OR KT= PRESCRIPTION DRUGS OR KT= DRUG #PRESCRIPTIONS
#2. REGULAT* OR REQUIR* OR RESTRICT* OR LEGISLAT* OR LAW? OR ACT? OR POLICY OR POLICIES
#3. COMPAR* OR EVALUAT* OR EFFECT?
#4. NARCO* OR CRIM* OR WAR? OR ADDICT* OR ABUS* OR TRAFFIC* OR ILLICIT*
#5. TI=MANUAL? OR TI=CANCER OR TI=REGISTRATION FILE OR TI=RETIRED REGISTRANTS
#6. (#1 AND #2 AND #3) NOT #4
#7. #6 NOT #5

Appendix 13. Search strategies: IPA

IPA, International Pharmaceutical Abstract, WebSPIRS
Search fields: A combination of 'Descriptors' and 'Terms Anywhere'
1.((approval*) in DE) or ((licensing) in DE) or ((licensure) in DE) or ((labeling) in DE) or ((classification) in DE) or ((patent*) in DE) or ((marketing) in DE) or ((advertising) in DE) or ((insurance) in DE) or ((reimbursement) in DE) or ((formularies) in DE) or ((formulary) in DE) or ((essential) in DE) or (reminder system*) or ((Education-pharmaceutical-continuing) in DE) or ((Education-continuing) in DE) or ((Hospitals-pharmacy-and-therapeutics-committee) in DE) or (drug* near1 monitoring) or ((Drugs-adverse-reactions-reports) in DE) or ((Reports-drugs-adverse-reactions) in DE) or ((Costs-drugs) in DE) or ((Pricing-drugs) in DE) or ((pharmacoeconomics) in DE) or (reference near2 pric*) or ((Costs-prescription-drugs) in DE) or ((purchasing) in DE) or (cost adj sharing) or ((copayment*) in DE) or (deductibles) or (coinsurance) or ((drug information services) in DE) or (patient adj education)

(regulat* or restrict* or control* or legislat* or law or laws or act or acts or policy or policies or program or programs) and (control* or compar* or evaluat* or time series or impact* or effect or effects) and ((sc=20) or (sc=22))
2.(regulat* or restrict* or control* or legislat* or law or laws or act or acts or policy or policies or program or programs) and (control* or compar* or evaluat* or time series or impact* or effect or effects) and ((sc=20) or (sc=22))
3.(1 and 2) not sc=6

Appendix 14. Search strategies:OECD

OECD (Organisation for Economic Co-operation and Development)
Searched: Publications & Documents, limited to OECD Publications only
drug or drugs or pharmaceutical or pharmaceuticals or medicaments or medicines or prescription or prescriptions or prescribe or prescribing

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Appendix 15. Search strategies: SourceOECD

SourceOECD Search fields: 'Title' or 'Abstract' drug or drugs or pharmaceutic* or medicament* or medicines or prescrip*or prescrib*

Appendix 16. Search strategies: World Bank Documents & Reports

World Bank Documents & Reports Limited to sectors: Health, Nutrition and Population or Hospitals, Secondary & Tertiary or Primary health or Reform and Financing drug or drugs or pharmaceutical or pharmaceuticals or medicament or medicaments or medicines or prescription or prescriptions or prescribe or prescribed or prescribing

Appendix 17. Search strategies: World Bank e-Library

World Bank e-Library Search fields: 'Title' or 'Abstract' or 'Keywords' drug or drugs or pharmaceutical or pharmaceuticals or pharmaceutic or pharmaceutics or medicament or medicaments or medicines or prescription or prescriptions or prescribe or prescribed or prescribing

Appendix 18. Search strategies: JOLIS

JOLIS, The Library Network, serving the World Bank Group and IMF Search field: 'Keywords Anywhere'. Search done in two separate stages keywords anywhere "prescrib$ or prescrip$" AND keywords anywhere "drug or drugs or pharmaceutic$ or medica$ or medicines" AND keywords anywhere "regulat$ or requirement$ or restrict$ or monitor$ or control$ or legislation$ or law? or act or acts or policy or policies or politics or reform$ or system? or plan or plans or planning or program? or strateg$ or incentive$"

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Appendix 19. Search strategies: Global Jolis

Global Jolis, online catalogue for the World Bank Country Office PIC/Libraries Search field: 'Words or Phrase'. Search done in two separate stages 1. prescrib$ or prescrip$ AND drug or drugs or pharmaceutic$ or medica$ or medicines AND regulat$ or requirement$ or restrict$ or monitor$ or control$ or legislation$ or law? or act or acts or policy or policies or politics 2. prescrib$ or prescrip$ AND drug or drugs or pharmaceutic$ or medica$ or medicines AND reform$ or system? or plan or plans or planning or program? or strateg$ or incentive$

Appendix 20. Search strategies: WHO

WHO (World Health Organisation), browsed The Essential Drugs and Medicines web site

Appendix 21. Search strategies: WHOLIS

WHOLIS, the WHO library database Search field: 'Words or phrase' words or phrase "prescrib$ or prescrip$" AND words or phrase "regulat$ or requirement$ or restrict$ or monitor$ or control$ or legislation$ or law? or act or acts or policy or policies or politics or reform$ or system? or plan or plans or planning or program? or strateg$ or incentive$"

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WHAT'S NEW

Last assessed as up-to-date: 13 May 2007.

Date	Event	Description
6 September 2011	Amended	Minor change to plain language summary

HISTORY

Review first published: Issue 3, 2007

Date	Event	Description
18 March 2009	Amended	Correction to typographical error.
12 November 2008	Amended	Minor changes
30 July 2008	Amended	Converted to new review format.
14 May 2007	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

MOA, AA and ADO prepared the protocol. JPK and HS commented on protocol drafts. HS, AA, MOA, and JPK applied the inclusion criteria, assessed the quality and extracted the data for the included studies. CR further developed quality criteria (based on the EPOC criteria) for interrupted time series (ITS) and repeated measures studies. CR and AV conducted statistical reanalyses for the ITS studies. HS prepared the first draft of the report. The others commented on and contributed to subsequent iterations.

DECLARATIONS OF INTEREST

MA has previously carried out short-term pharmacoeconomic projects for the National Insurance Service and the Norwegian Medicines Agency. From 1997-1999 he worked for a private company, Brevreklame, doing market research for pharmaceutical firms in Norway.

HS was supported by the Dutch Health Care Insurance Board (CVZ).

JPK has previously worked one year each for the Danish Medicines Agency and Lundbeck A/S as part of a residency in clinical pharmacology and is currently employed five hours a week at the Danish Medicines Agency (Licensing Division).

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INDEX TERMS

Medical Subject Headings (MeSH)

*Drug Costs; *Economics, Pharmaceutical; *Reimbursement, Incentive; Budgets; Drug Utilization [*economics]; Health Care Costs; Health Expenditures; Health Services [standards; utilization]

MeSH check words

Humans

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